



## Selección de Resúmenes de Menopausia

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### **Microfat and Nanofat Grafting in Genital Rejuvenation.**

Menkes S, SidAhmed-Mezi M1, Meningaud JP1, Benadiba L, Magalon G2, Hersant B1.

**BACKGROUND:** Genitourinary syndrome of menopause (GSM) is a major problem in many post- or perimenopausal women. Lipofilling has long been considered to be an effective technique for restoring volume, but the discovery of its trophic properties has made it the most widely used method in regenerative medicine. **OBJECTIVES:** Microfat and nanofat grafting is a new technique. In this study, we aimed to assess the safety and efficacy of microfat and nanofat grafting for vulvovaginal rejuvenation. **METHODS:** Women with GSM and who met the inclusion criteria were enrolled. Women received microfat in the labia majora and nanofat in the vagina; follow-up was conducted 1, 3, 6, 12, and 18 months after treatment. The vaginal health index (VHI) and Female Sexual Distress Scale-Revised (FSDS-R) were used to assess improvement in vulvovaginal atrophy, orgasm, and sexual desire post-treatment. **RESULTS:** Fifty women were included in this study; their average age was 53 years (range, 45-63 years). The VHI score significantly increased at 1 and 3 months after treatment ( $p < 0.0001$ ). Moreover, the average FSDS-R score showed a significant improvement at 1- and 3-months post-treatment. This score stabilized from 6 to 12 months but showed further improvement at 18 months. At 6 months post-treatment, for both the scales, data pertaining to 80% of patients appeared normalized. There was a particular benefit noted for dryness and dyspareunia. At 18 months, the results remained stable for all of the patients. No major side-effects were observed. **CONCLUSIONS:** There are now many ways to rejuvenate the intimate sphere, but microfat and nanofat grafting seem to offer good results with an autologous procedure. Their use appears promising for genital rejuvenation.

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### **A multicenter, randomized study to select the minimum effective dose of estetrol (E4) in postmenopausal women (E4Relief): part 1. Vasomotor symptoms and overall safety.**

Gaspard U, Taziaux M, Mawet M, Jost M, Gordenne V, Coelingh Bennink HJT, Lobo RA, Utian WH, et al.

**OBJECTIVE:** The aim of this study was to select the minimum effective dose of estetrol (E4) for the treatment of vasomotor symptoms in postmenopausal women. **METHODS:** This was a multicenter, randomized, double-blind, placebo-controlled study. Postmenopausal women ( $n=257$ , of whom 32 were hysterectomized) aged 40 to 65 years, with  $\geq 7$  moderate to severe hot flashes (HFs) per day, or 50 or more moderate to severe HFs weekly, received 2.5, 5, 10, or 15 mg E4, or placebo once-daily for a period of 12 weeks. Efficacy was assessed by recording the frequency and severity of HFs. Overall safety was assessed by recording adverse events, measuring endometrial thickness, and monitoring bleeding patterns. Treatment groups were compared using analysis of covariance. **RESULTS:** The frequency of moderate to severe HFs decreased with all E4 doses. The difference in the percentage change of weekly HF frequency was significant for 15 mg E4 versus placebo at both W4 (-66% vs -49%,  $P=0.032$ ) and W12 (-82% vs -65%,  $P=0.022$ ). The decrease in severity of HFs was significantly more pronounced for 15 mg E4 than for placebo at both W4 (-0.59 vs -0.33,  $P=0.049$ ) and W12 (-1.04 vs -0.66,  $P=0.049$ ); the other doses failed to achieve statistical significance. In nonhysterectomized women, endometrial thickness increased during treatment and normalized following progestin treatment at study completion. No endometrial hyperplasia was observed. **CONCLUSIONS:** Estetrol 15mg is considered to be the minimum effective daily oral dose for treatment of vasomotor symptoms. Its current seemingly favorable safety profile is further to be confirmed in phase 3 clinical development.

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### **Effect of progestogen-only contraception on premenopausal fracture risk: a case-control study.**

Kyvernitakis I1,2,3, Kostev K4, Thomasius F5, Stumpf U6, Hadji P7,5.

Our study demonstrated that progestogen-only oral and intrauterine contraceptives are not associated with fracture risk independent from age. **PURPOSE:** The use of progestogen-only contraception, resulting in a hypoestrogenic state, has been associated with impaired bone acquisition and increased fracture risk. The aim of this large population-based study was to assess the fracture risk in association with the use of progestogen-only contraceptives (progestogen-only pills (POPs) and progestogen-containing IUDs (LNG-IUD)). **METHODS:** We identified 14,421 women between 16 and 55 years of age with a first-time diagnosis of fracture and matched them with 14,421 random controls using the Disease Analyzer Database. **RESULTS:** The results of the first adjusted logistic regression model (ever use vs. never use of progestogen-only contraceptives) revealed that there was no significant association between the use of POPs (OR = 0.98, 95% CI 0.90-1.07,  $p = 0.657$ ) or LNG-IUDs (OR = 0.99, 95% CI 0.81-1.21,  $p = 0.945$ ) and fracture incidence. Also, in the second regression model, we observed no effect of duration of use of POPs (OR = 1.01, 95% CI 0.98-1.03,  $p = 0.672$ ) or LNG-IUDs (OR = 0.94, 95% CI 0.87-1.02,  $p = 0.177$ ) on fracture occurrence. We also observed no effect in different age groups. **CONCLUSION:** Our study results indicate that progestogen-only contraception (either POPs or LNG-IUDs) is not associated with fracture risk and may be considered a bone-safe option for adults and adolescents.

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### **The relationship of 25-hydroxyvitamin D values and risk of fracture: a population-based retrospective cohort study.**

Aul AJ1, Dudenkov DV2, Mara KC3, Juhn YJ4, Wi CI4, Maxson JA5, Thacher TD6.

Our study investigates 25-hydroxyvitamin D levels and fracture risk using population-level data. 25-Hydroxyvitamin D values < 12, 12-19, and > 50 ng/mL were not associated with increased risk of fractures overall compared with values 20-50 ng/mL. Severely low levels may be associated with increased risk of osteoporotic fracture, particularly of the wrist. **INTRODUCTION:** Studies of the relationship between serum 25-hydroxyvitamin D (25(OH)D) levels and fracture risk have been inconsistent. We hypothesized that high 25(OH)D concentrations (> 50 ng/mL) would be associated with increased risk of fracture. **METHODS:** We identified all adult patients living in Olmsted County, Minnesota, between January 1, 2005 and December 31, 2011, who had at least one 25(OH)D measurement. Fracture outcomes were retrieved starting 30 days after 25(OH)D measurement and until patients' final clinical visit as an Olmsted County resident, December 31, 2014, or death. Data were analyzed using Cox proportional hazard regression. **RESULTS:** Of 11,002 individuals with a 25(OH)D measurement, 5.8% had a 25(OH)D value < 12 ng/mL, and 5.1% had a value > 50 ng/mL. Compared with subjects with 25(OH)D values 20-50 ng/mL (reference group), values < 12, 12-19, and > 50 ng/mL displayed no association with overall fracture risk. After adjusting for a prior diagnosis of osteoporosis/osteopenia, only individuals with values < 12 ng/mL had increased risk of any osteoporotic fracture (aHR = 1.41; 95% CI 1.05-1.89) and wrist fracture (aHR = 2.11; 95% CI 1.27-3.48) compared with the reference group. Compared with the reference group, values < 12 ng/mL were associated with increased risk of any fracture (aHR = 1.35; 95% CI 1.01-1.80), osteoporotic fracture (aHR = 2.18; 95% CI 1.44-3.31), and wrist fracture (aHR = 2.39; 95% CI 1.19-4.81) in subjects without a prior diagnosis of osteoporosis/osteopenia, but not in those with a prior diagnosis of osteoporosis/osteopenia. **CONCLUSION:** Severely low 25(OH)D levels may be associated with increased risk of osteoporotic fracture, particularly of the wrist, but 25(OH)D values > 50 ng/mL were not associated with increased fracture risk.

**Health Qual Life Outcomes. 2020 May 6;18(1):123. doi: 10.1186/s12955-020-01377-1.**

### **Relationship of different intensities of physical activity and quality of life in postmenopausal women.**

Felipe J1, Viesel J2, Reis AD2, da Costa Barros EA3, de Paulo TRS4, Neves LM5, Júnior IFF6.

**BACKGROUND:** It is known that the elderly population remains most of the time in light activity. Physical activity plays a key role in the primary prevention of chronic diseases to mitigate various deleterious effects of aging and improve quality of life. The objective of the present study was to evaluate whether the time that postmenopausal women remain in light activities during the day are related to better quality of life and compare these results with the quality of life of those who remain longer in moderate intensity and vigorous activity. **METHODS:** This is a cross sectional study there were evaluated 102 women, aged 50 to 79 years, all postmenopausal. Physical activity was measured by triaxial accelerometers. The quality of life was assessed using a Brazilian validated version of the SF-36 questionnaire. The sample was divided in three groups (G1, G2 and G3) according to tercile of time spent per week on light, moderate and moderate+vigorous physical activity. The comparisons between groups were made by ANOVA One Way, and the relationship between variables were made through the Spearman's correlation coefficient, and the significance was set

at 5%. RESULTS: We found that the amount of time of light physical activity shows a higher correlation values compared to the moderate and moderate+vigorous physical activity ( $p < 0,05$ ) and presented significant correlation in all domains of quality of life. Vigorous physical activity did not presented significant correlation in all domains of quality of life. CONCLUSION: Our data suggests that light intensity physical activity presented influence on the quality of life of postmenopausal women.

**Nutrients. 2020 May 4;12(5). pii: E1310. doi: 10.3390/nu12051310.**

### **Circulating Levels of Muscle-Related Metabolites Increase in Response to a Daily Moderately High Dose of a Vitamin D3 Supplement in Women with Vitamin D Insufficiency-Secondary Analysis of a Randomized Placebo-Controlled Trial.**

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Recently, we demonstrated negative effects of vitamin D supplementation on muscle strength and physical performance in women with vitamin D insufficiency. The underlying mechanism behind these findings remains unknown. In a secondary analysis of the randomized placebo-controlled trial designed to investigate cardiovascular and musculoskeletal health, we employed NMR-based metabolomics to assess the effect of a daily supplement of vitamin D3 (70  $\mu\text{g}$ ) or an identically administered placebo, during wintertime. We assessed the serum metabolome of 76 postmenopausal, otherwise healthy, women with vitamin D (25(OH)D) insufficiency (25(OH)D  $< 50$  nmol/L), with mean levels of 25(OH)D of  $33 \pm 9$  nmol/L. Compared to the placebo, vitamin D3 treatment significantly increased the levels of 25(OH)D (-5 vs. 59 nmol/L, respectively,  $p < 0.00001$ ) and 1,25(OH)2D (-10 vs. 59 pmol/L, respectively,  $p < 0.00001$ ), whereas parathyroid hormone (PTH) levels were reduced (0.3 vs. -0.7 pmol/L, respectively,  $p < 0.00001$ ). Analysis of the serum metabolome revealed a significant increase of carnitine, choline, and urea and a tendency to increase for trimethylamine-N-oxide (TMAO) and urinary excretion of creatinine, without any effect on renal function. The increase in carnitine, choline, creatinine, and urea negatively correlated with muscle health and physical performance. Combined with previous clinical findings reporting negative effects of vitamin D on muscle strength and physical performance, this secondary analysis suggests a direct detrimental effect on skeletal muscle of moderately high daily doses of vitamin D supplements.