CONCLUSION: These results provide the first evidence that twins are more prone to an early natural menopause than singletons. Furthermore, they reveal many cases in which the ovarian lifespan was truncated in only one member of a MZ or DZ pair. Although causal explanations for these findings are not yet fully apparent, and may differ with zygosity, there was greater concordance between menopausal ages of MZ and than DZ twins, as expected. We hypothesize that the findings reflect differences in the size of the ovarian follicle store established before birth.

Supported by: None

Wednesday, October 19, 2005
3:45 p.m.

O-289

Baseline Vasomotor Symptoms and Cardiovascular Events Among Postmenopausal Women Using Conjugated Equine Estrogens (CEE) or CEE Plus Medroxyprogesterone (MPA) in the Women's Health Initiative (WHI) Clinical Trials. D. H. Barad, M. L. Stefanick, B. Cochrane, V. Barnabei, R. Brunner, J. Rossouw. Albert Einstein College of Medicine, Bronx, NY; Stanford University, Stanford, CA; Fred Hutchinson Cancer Research Center, Seatle, WA; Medical College of Wisconsin, Milwaukee, WI; University of Nevada School of Medicine, Reno, NV; NHLBI, Washington, DC.

OBJECTIVE: The objective of this paper is to evaluate the possible association and interactions of vasomotor symptom status (VMS) at baseline and hormone treatment with cardiovascular outcomes.

DESIGN: Analysis of baseline and follow up data from a randomized clinical trial of hormone treatment in postmenopausal women

MATERIALS AND METHODS: The study group for this analysis was the 27,347 women participating in the WHI hormone randomized clinical trials. Eliminating 13% of subjects with missing or ambiguous data left 23,779 for analysis. Cox regression models were computed for all subjects, and also by hormone trial component either unadjusted or adjusted for cardiovascular disease (CVD) risk factors measured at baseline [age, prior hormone use (none, <5, 5-10, >10 years), BMI, left ventricular hypertrophy, current cigarette smoking, hypertension (using antihypertensive medications or blood pressure >140/90), treated diabetes, treated high cholesterol levels, parental history of CVD (premature MI (<55 in father or <65 in mother) or parental history of stroke)]. Separate Cox regression models were also performed for each hormone trial component: the Estrogen+Progestin trial of combined conjugated equine estrogen (CEE) and medroxyprogesterone acetate (MPA) or placebo in women with an intact uterus and the Estrogen-Alone trial of CEE or placebo in women with a hysterectomy prior to baseline.

RESULTS: Hormone Trial participants reported their vasomotor symptom status as follows: Never VMS=6,993 (29.4%; HT 3,514; placebo 3,479); Past VMS=7,697 (32.4%; HT 3,848; placebo 3,849); and Baseline VMS=9,089 (38.2%; HT 4,527; Placebo 4,562). Mild to severe vasomotor symptoms were reported at baseline by 48% of women 50 to 59 years, 39.5% of women 60 to 69 years, and 12% of women 70 to 79 years. We found no evidence of a significant interaction between hormone treatment and the presence of VMS at baseline or prior VMS in the unadjusted models. However, when analyzed by trial component, unadjusted hazard ratios (95% confidence limits) for CHD in the CEE group of the Estrogen-Alone trial were as follows: Never VMS 0.71 (0.48, 1.04); Past VMS 1.05 (0.71, 1.54); and Baseline VMS 1.40 (0.98, 1.98) (p for interaction = 0.036). After adjusting for the cardiovascular risk factors there was no evidence of any significant interaction.

CONCLUSION: The presence of vasomotor symptoms reported at initiation of hormone treatment or in the past does not affect postmenopausal women's risk for CHD. The trend noted for an increased risk for CHD associated with vasomotor symptom history among women taking CEE deserves further analysis.

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Wednesday, October 19, 2005
4:00 p.m.

O-290

The Cognitive/Psychological Effect of Dose Titrated DHEA Supplementation in Post-Menopausal Women. M. B. Amin, J. E. Buster, P. Callas, N. Burger, M. Pisarska, P. R. Casson. University of Vermont, Burlington, VT; Baylor College of Medicine, Houston, TX; Cedars-Sinai, UCLA School of Medicine, Los Angeles, CA.

OBJECTIVE: To evaluate the effect of physiologic oral DHEA (dehydroepiandrosterone) administration on cognitive/psychological function in a group of post-menopausal women with low endogenous DHEA-S levels.

DESIGN: Randomized, double-blinded, parallel, placebo-controlled trial with a dose titration protocol. The trial lasted one year.

MATERIALS AND METHODS: Twenty-two post-menopausal women with low endogenous DHEA-S levels were randomized to DHEA treatment (n=11) and placebo (n=11), given at 8: 00 AM. The subjects were non-smokers and not on HRT. The treatment group was given a 40 mg daily dose of oral micronized DHEA (courtesy Belmar pharmacy, Lakewood CO) for one year, with monthly dose titration by an un-blinded investigator to maintain levels of DHEA-S between 300 and 450 microgram/dL. Serum samples for DHEA, DHEA-S, and Testosterone (T) were drawn immediately before DHEA administration and batch assayed using commercially available assays (DSL Ltd. Webster TX). Outcomes were measured using 7 validated cognitive function tests: Geriatric Depression Scale (GDS), Trail Making A (TMA), Trail Making B (TMB), Digit Symbol (DS), Word List Recall (WLR), Controlled Oral Word Association (COWA), and Life Satisfaction Index-A (LSI-A). The primary outcomes were the scores on these tests, which were given at 0, 3, 6, and 12 months. Statistical analysis was performed using mixed-model ANOVA.

RESULTS: There were no statistically significant differences in cognitive function scores between the two groups on 5 of the 7 measures. In the DS test, the treatment group showed a subtle but statistically significant improvement over time when compared to the subjects in the placebo group (p=0.006). In the LSI-A, the placebo group showed a slight decrease in scores over time when compared to the treatment group (p=0.04).

CONCLUSION: Physiologic dose-titrated replacement of DHEA in post-menopausal women with low endogenous DHEA-S levels does not result in marked improvement in cognitive function. In this study, the DHEA-treated group showed only a slight benefit in 2 of the 7 parameters measured. While this study is limited by small numbers, the carefully selected subjects, the long study duration, the titrated dose regimen, and the multiple time points of outcome measurement, all strengthen the contention that the cognitive/psychological effect of DHEA, while it very well may exist, is not dramatic. Considering the recent enthusiasm surrounding the use of DHEA to slow cognitive decline and the conflicting studies that have been published, more study is necessary before the clinical use of DHEA for purposes of preventing or ameliorating cognitive impairment can be advocated.

Supported by: None.

Wednesday, October 19, 2005
4:30 p.m.

O-291

Raloxifene Shows Progestagenic Effects on Thrombospondin-1 (TSP-1) and Down-Regulation of Progesterone Receptors in a Human Endometrial Cell Line. S. M. Bocca, D. F. Archer. The Jones Institute for Reproductive Medicine, Eastern Virginia Medical School, Norfolk, VA.

OBJECTIVE: To determine if the effects of raloxifene (Rlx) on TSP-1 are mediated through the estrogen receptor (ER) or progesterone receptor (PR). Angiogenesis is regulated by a balance between pro-angiogenic (VEGF) and antiangiogenic (TSP-1) proteins. VEGF mRNA and protein are upregulated by E, blocked by specific E-antagonists and only minimally increased by P in human endometrial cells; whereas for TSP-1 mRNA is stimulated by P with the effect being blocked by the anti-P mifepristone (RU 486). Estradiol does not stimulate TSP-1 expression in these cells. Raloxifene is a selective ER modulator that acts as an E-agonist on bone and lipid metabolism but as an E-antagonist in the breast and the uterus. The