DESIGN: Prospective, placebo-controlled, double-blinded, randomized 6-month trial.

MATERIALS AND METHODS: Thirty-two postmenopausal women were randomized to either HRT consisting of 0.625 conjugated equine estrogens plus 2.5 mg medroxyprogesterone acetate (n=16) or placebo (n=16). Insulin sensitivity was measured by the euglycemic hyperinsulinemic clamp at baseline and after 6 months of treatment and was corrected per kilogram of lean body mass. C-reactive protein (CRP) and interleukin-6 (IL-6) were measured by ultra-sensitive enzyme-linked immunoassay. Lean body mass was measured by dual-photon x-ray absorptiometry.

RESULTS: There were no significant differences between the two groups with regard to age, weight, lean body mass or insulin sensitivity corrected per kg of lean body mass at baseline. CRP decreased in both the placebo and the HRT groups (-0.23 μg/mL and -1.36 μg/mL, respectively). IL-6 increased in both the placebo and the HRT groups (0.12 pg/mL and 0.17 pg/mL, respectively). Insulin sensitivity increased less in the HRT group compared to the placebo group (0.29 mg/min/kg and 0.91 mg/min/kg, respectively). For all patients, the change in IL-6 was negatively related to the change in insulin sensitivity ($r = -0.36$, $p = 0.04$). In the HRT group, there was a trend toward a negative relationship between change in CRP and change in insulin sensitivity ($r = -0.43$, $p = 0.09$). There was no relationship between the change in IL-6 and the change in insulin sensitivity in the HRT group ($r = -0.10$, $p = 0.70$). In the placebo group, the change in IL-6 was negatively related to the change in insulin sensitivity ($r = -0.61$, $p = 0.01$). There was no relationship between the change in CRP and the change in insulin sensitivity in the placebo group ($r = 0.28$, $p = 0.29$).

CONCLUSION: Changes in IL-6 correlate with changes in insulin sensitivity in postmenopausal women. CRP correlates better with changes in insulin sensitivity in postmenopausal women taking HRT.

Supported by: National Institutes of Health: R29 AG151121 and M01 RR109

Tuesday, October 19, 2004
5:15 P.M.

O-168

Pharmacokinetics of testosterone gel in bilaterally oophorectomized women. J. S. Archer, P. Malcom, R. J. Chang. University of California-San Diego, La Jolla, CA.

OBJECTIVE: Evaluate the pharmacokinetics of two doses of a topical testosterone gel in surgically menopausal women.

DESIGN: Prospective randomized study.

MATERIALS AND METHODS: Six bilaterally oophorectomized women (mean age 48.3; range 38–53) with agonadal serum free testosterone (T) levels (mean 1.28 pg/ml) were randomized to either 0.6 or 1.2 gm dose of a 1% T gel. Gel was applied daily to the outer thigh for 28 days. Five of the six women were on different estrogen therapies during the study. Volunteers were admitted to the hospital on days 1, 7 and 28 of T treatment and peripheral blood samples were obtained at -0.5, 0, 0.5, 1, 2, 3, 4, 6, 9, 12 and 24 hours after application. Serum levels of total T, free T, SHBG, estrone (E1) and estradiol (E2) were determined at each time point by radioimmunoassay. Area under the curve (AUC) for free T was calculated using the trapezoidal method.

RESULTS: Free T levels achieved steady state in 3 women on application day 7 while the other volunteers continued to have increases in serum free T until day 28 regardless of the dose of T gel used. There was a wide range in AUCs among the volunteers (0.02–20.23 pg/ml). The one woman not on estrogen had the highest level of free T. Both E1 and E2 remained unchanged during the study while SHBG levels dropped.

Day of Blood Draw	Free T (pg/ml)	Total T (nMol/L)	E1 (pMol/L)	E2 (pMol/L)	SHBG (nMol/L)
Baseline	1.16	0.68	442	152	58.6
Day 7	1.95	3.57	499	150	54.8
Day 28	2.91	4.80	557	163	48.9

CONCLUSION: There is interindividual variation among women both in the amount and timing of T gel absorption. Dosing of supplemental T should be individualized using serum T levels. Concomitant estrogen therapy appears to decrease serum free T when using a transdermal T gel.

Supported by: North American Menopause Society

Tuesday, October 19, 2004
5:30 P.M.

O-169

Individual dose response of insulin resistance to estrogen therapy. K. Jovanovic, H. S. Taylor. Yale University School of Medicine, New Haven, CT.

OBJECTIVE: The effect of estrogen therapy on insulin resistance is controversial. Conflicting reports suggest that estrogen may increase or decrease insulin resistance depending on dose and BMI. Reports demonstrating no effect may be an average of individual increases and decreases. Here we determine the dose response of insulin resistance to estrogen dose in individual patients who had undergone surgical menopause.

DESIGN: Prospective cohort trial

MATERIALS AND METHODS: We identified all patients from the gynecology clinic and gynecologic oncology services who underwent Bilateral Salpingo-Oophorectomy at Yale-New Haven Hospital from 1/1/00 to 6/30/02. Chart review and pathologic verification identified 1468 patients. Ninty patients met inclusion criteria which included absence of diabetes and no contraindication to estrogen therapy; these individuals were recruited by telephone. 14 patients were enrolled in the variable dose trials and 5 completed the study. Each subject was treated for three months with 0.3 mg, 0.625 mg and 1.25 mg of conjugated equine estrogens (CEE) in random order, for a total of nine months of treatment. At the end of each dosing regimen fasting serum insulin and glucose were obtained.

RESULTS: Fasting glucose to insulin ratio and QUICKI were calculated. No significant change was noted in either parameter with any dose of CEE among individuals. ($P>0.05$) All three doses also did not change insulin resistance when compared on a mg/kg basis ($P>0.05$). Subjects with a BMI$>$ 30 or with BMI$<$25 all demonstrated a lack of dose response.

CONCLUSION: This is the first study to examine the dose response of insulin resistance to estrogen in individuals. Though the power of the study is small, the results show that insulin resistance does not vary significantly within individual patients when doses of estrogen are considerably altered. Insulin resistance should not factor into decisions regarding estrogen dosing.

Supported by: None

Tuesday, October 19, 2004
5:45 P.M.

O-170

Raloxifene improves vaginal maturation index in vaginal smears of postmenopausal osteoporotic women. H. B. Zeyneloglu, M. Oktem, A. N. Haberal, I. Esinler, E. Kuscu. Baskent University, Department of Obstetrics and Gynecology, Ankara, Turkey; Baskent University, Department of Pathology, Ankara, Turkey.

OBJECTIVE: To analyze the effect of raloxifene on urogenital atrophy, vaginal PH and vaginal smear among postmenopausal osteoporotic women.

DESIGN: Prospective, randomized study

MATERIALS AND METHODS: A total of sixty healthy postmenopausal osteoporotic women were included in the study. Inclusion criteria limited patients to those with body mass index < 30 kg/m^2, no malignancy, no pathologic findings in gynecologic examination or on cervical smear, no systemic or vaginal estrogen therapy or vaginal moisturizer 6 months prior to the study. Patients were randomized into two groups: Group I (N=30) included patients treated with raloxifene 60 mg/day (Evista, Lilly, Istanbul, Turkey) and Group II (N=30) which included patients treated with risedronate 5 mg/day (Actonel, Aventis Pharma, Istanbul Turkey) served as controls. Urogenital atrophy was recorded and their sensitivity assessed on a scale from 1 to 4 (1= severe 2=moderate, 3=mild, and 4=none). Vaginal pH was measured by using a pH test strip (Universal indikator Ph 0–14, Merck KGaA, 64271 Darmstadt, Germany) and vaginal smear test was performed from upper lateral vaginal wall at the same time. A pathologist blinded to patients' groups and information evaluated vaginal smear test by vaginal maturation index formulated as (0.2$\times$ percent parabasal cells + 0.6$\times$ percent intermediate cells + 1.0$\times$ percent superficial cells). The primary end point of the study was decided to be the vaginal maturation index. The secondary end points were noted as vaginal pH and the score for urogenital atrophy. All primary and secondary end points were assessed