

0.01), for daidzein ($p = 0.004$), for glycitein ($p = 0.005$), for dihydrodaidzein ($p = 0.002$), and for O-desmethylnangiolensin ($p = 0.03$). However, there were no differences between groups in changes in CRP, IL-6, TNF- α , leptin, or adiponectin.

CONCLUSION: We conclude that the CRP and adiponectin are significantly related to intraabdominal fat and total abdominal fat in postmenopausal women. Although soy phytoestrogen supplementation increases serum levels of isoflavones, serum CRP, IL-6, TNF- α , leptin, and adiponectin do not appear to be affected.

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Wednesday, October 25, 2006
4:30 pm

O-212

THE EFFECT OF ESTROGEN ON EDHF FUNCTION IN THE MESENTERIC VASCULAR SYSTEM. N. Z. Burger, G. Osol, N. Gokina. Univ of Vermont, Burlington, VT.

OBJECTIVE: To explore the effects of estrogen deficit and replacement on the vasodilatory action of endothelium-derived hyperpolarizing factor (EDHF) in the rat mesenteric vasculature.

DESIGN: Cohort study.

MATERIALS AND METHODS: Third order mesenteric vessels were harvested from OVX (oophorectomy only) and OVX-E (oophorectomy with 17 β -estradiol replacement) female rats. Following inhibition of nitric oxide synthase (NOS) and cyclo-oxygenase (COX), vessels were pre-constricted with phenylephrine (Phe). Increasing concentrations of acetylcholine (Ach) were added to identify the vasodilatory activity of endothelium-derived hyperpolarizing factor (EDHF). The transient and sustained responses of each vessel to each Ach concentration were recorded. The Ach concentration required to achieve 50% of maximal vessel diameter (EC_{50}) was calculated for each vessel.

RESULTS: The OVX & OVX-E groups did not differ significantly in age (97 ± 0.8 days and 96.7 ± 1.3 days; $p=0.83$). There were significant differences in body weight (263.4 ± 12 mg and 215.3 ± 8.4 mg; $p=0.009$) and in uterine weight (0.15 ± 0.014 mg and 0.71 ± 0.06 mg; $p=0.001$). There was a significant difference in the transient EC_{50} between the OVX & OVX-E groups (0.4 ± 0.09 μ M and 0.17 ± 0.03 μ M; $p=0.05$). There was a significant difference in the sustained EC_{50} between the OVX & OVX-E groups (0.4 ± 0.09 μ M and 0.19 ± 0.04 μ M; $p=0.05$).

CONCLUSION: Estrogen increases EDHF-mediated vasodilatation in the mesenteric vasculature of the rat.

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4:45 pm

O-213

SKELETAL AND UTERINE EFFECTS OF BAZEDOXIFENE IN OVARECTOMIZED MICE AND RATS WITH COMPARISON TO RALOXIFENE AND LASOFOXIFENE. Y. P. Kharode, P. V. Bodine, F. J. Bex, B. S. Komm. Wyeth Pharmaceuticals, Collegeville, PA.

OBJECTIVE: To evaluate the effects of oral administration of bazedoxifene (BZA), raloxifene (RAL), and lasofoxifene (LAS) on bone and uterine endpoints.

DESIGN: Preclinical study utilizing mice, ovariectomized (ovx) mice, or ovx rat osteopenia models. C57BL6 mice or Sprague-Dawley rats were obtained from Charles River (Wilmington, MA). 8-10 animals were used per dose group.

MATERIALS AND METHODS: Animals received daily oral treatments of BZA (0.1 mg/kg, 0.3 mg/kg, 1.0 mg/kg, 3.0 mg/kg, and 10 mg/kg) or vehicle for 42 (rats) or 60 (mice) days. Bones were analyzed using peripheral quantitative computed tomography (pQCT) and/or μ CT. In comparative studies, animals received BZA (0.3 mg/kg), RLX (3.0 mg/kg), LAS (3.0 mg/kg), ethinyl estradiol (0.3 mg/kg), or vehicle. Uterine evaluation in-

cluded wet weight changes, histology, and complement component 3 gene expression.

RESULTS: Untreated ovx mice show significant bone loss in comparison to sham (392 ± 8 mg/cm³ vs. 479 ± 8 mg/cm³ and 93 ± 5 mg/cm³ vs. 149 ± 5 mg/cm³ for total and trabecular densities, respectively). Post-treatment total (466 to 502 mg/cm³) and trabecular vBMD (121 to 136 mg/cm³) measured by pQCT significantly increased in all treatment groups compared to the ovx + vehicle group. Uterine weight in the ovx group (16 ± 1 mg) was significantly lower than that for the sham group (65 ± 5 mg, $p<0.01$), as were all doses of BZA except for 0.1 mg. In intact mice, 0.3 mg/kg/day ethinyl estradiol (EE) significantly increased total and trabecular BMD and uterine weight compared to the ovx group. Post-treatment femoral evaluation of intact mice revealed that all treatment groups had significant accrual of trabecular bone. BZA, RAL, and LAS significantly decreased while EE significantly increased serum cholesterol. Uterine weights were lower in the BZA group (BZA [46 ± 1 mg] $p<0.05$ vs vehicle [68 ± 5 mg]; RAL [64 ± 3 mg]; LAS [53 ± 2 mg]) and were significantly higher in EE group (198 ± 12 mg) compared to vehicle. In ovx rats, all three SERMs increased BMD compared to ovx controls ($p<0.05$), however BZA demonstrated a superior histomorphometric profile (increased bone area 1% >RAL). This correlated with statistically significant improvement in lumbar resistance to compressive forces ($p<0.05$). While BZA had little effect on any uterine endpoint, RAL and LAS stimulated statistically significant changes in uterine wet weight and notable changes in uterine histology. LAS demonstrated the poorest uterine profile.

CONCLUSION: Our results indicate that in C57BL mice, BZA prevented ovx-induced osteopenia without causing uterine stimulation. The beneficial effect of BZA on bone was confirmed in ovx rats, where BZA was also associated with less uterine stimulation than RAL or LAS. In the intact mice, BZA, RAL, and LAS produced accrual of bone, and significantly reduced serum cholesterol, but only BZA exhibited significant anti-estrogenic effects on the uterus. The mechanisms responsible for these SERMs to increase bone mass may be osteogenic, but further work is needed. In conclusion, BZA is a novel SERM with tissue-selective effects that may offer selective skeletal protection without uterine stimulation under quite different physiologic conditions.

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NURSES PROFESSIONAL GROUP

Wednesday, October 25, 2006
3:00 pm

O-214

CORRELATION OF SUBJECTIVE SYMPTOMS IN WOMEN WITH SYMPTOMATIC LEIOMYOMA WITH HEMATOCRIT AND UTERINE SIZE. W. Blocker, T. Nansel, C. Potlog-Nahari, A. Armstrong, L. Nieman. Reproductive Biology and Medicine Branch, Bethesda, MD; Div of Epidemiology, Statistics and Prevention Research; NICHD, Bethesda, MD; National Institutes of Health, Bethesda, MD.

OBJECTIVE: The purpose of this study was to evaluate whether subjective symptoms in women with symptomatic leiomyomata correlate with objective measurement of hematocrit and uterine size.

DESIGN: Observational cohort study.

MATERIALS AND METHODS: Women with symptomatic leiomyomata seeking treatment completed the Uterine Fibroid Symptom-Quality of Life (UFS) and the Short Form-36 Health Survey (SF-36) questionnaires. The UFS is a validated disease-specific questionnaire that assesses symptom severity and symptom impact on health-related quality of life (QOL). The SF-36 is a validated generic QOL survey. Concurrently, uterine size and hematocrit (Hct) were measured. Pearson's correlation coefficient was used to assess the relationship of Hct and uterine size with overall UFS symptom and QOL summary scales and the SF-36 physical and mental component summary scales and subscales. Other correlations included: Hct and the UFS questions related to bleeding symptoms, uterine size and the UFS questions related to pain/pressure symptoms, and the results among the two questionnaires. A p-value of < 0.05 was considered significant.

RESULTS: Subjects were 50 women aged 34 to 50 years (39 Black, 7 White, 2 Asian, 2 unknown). Each completed the SF-36 questionnaire and 34 completed the UFS questionnaire. Mean Hct was 34.4% (range 17.9 -