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The Possible Attenuating Effects of Estrogen on Circadian Blood Pressure Variation Using 24 Hour Ambulatory Monitoring S.R. LindHeim*, R. Freeman*, B. Witt*, D.H. Barad*, The Albert Einstein College of Medicine, 1300 Morris Park Avenue, Bronx, New York 10461

Objective: Blood pressure follows a circadian pattern with pressures highest in midmorning and progressively falling throughout the remainder of the day. Elevated blood pressure is a major predisposing factor for cerbro and cardiovascular morbidity and mortality which is believed to be precipitated by rapidly increasing arterial blood pressure upon awakening. We sought to evaluate the effects of oral and transdermal estrogen therapy on circadian variation of blood pressure in postmenopausal (PM) women. **Design:** A prospective nonrandomized trial. **Methods:** Twenty-four hour ambulatory blood pressure monitoring using a Spacelabs model 90202 monitoring device was performed on 18 PM women. Each were then placed on conjugated equine estrogen (CEE) (0.625 mg qd 1-25) or transdermal estrogen (TE2) (0.1 mg for three weeks each month) with added medroxyprogesterone acetate (5 mg qd 16-25 q monthly). Repeat 24 hour monitoring was performed during the estrogen phase of replacement during the 12th month of treatment. **Results:** For CEE and TE2, the mean age and BMI were 51.0 +/- 3.1 and 48.0 +/- 2.2; and 24.9 +/- 1.6 and 30.1 +/- 1.9 (p=0.053), respectively. All patients were menopausal confirmed with mean serum FSH of 88.7 +/- 11.2 mIU/ml. Prior to treatment, hemodynamic parameters followed a circadian pattern for all subjects with significantly higher mean diastolic pressure (DBP) during daytime (6 am to 6 pm) and lowest during nighttime (6 pm to 6 am) 83.0 +/- 2.1 vs 72.1 +/- 2.9 mmHg, p<0.05. Following CEE treatment, there was an attenuation in the differences between daytime and nighttime DBP (23.7+/- 4.8% increase pretreatment vs 2.4 +/- 6.8% increase posttreatment, p<0.01), MAP (19.8 +/- 4.5% increase vs 6.2 +/- 1.8%, p<0.05), and HR (11.3 +/- 3.5% increase vs 4.1 +/- 2.8%, p-NS. Following TE2, rises in daytime MAP reduced from 10.8 +/- 1.7 pretreatment to 4.9 +/- 4.1% post treatment, p=0.08. **Conclusion:** This preliminary study suggests that estrogen may confer cardiovascular benefit through an attenuation in rises of daytime hemodynamic changes. Currently, an ongoing prospective placebo controlled study is further evaluating this finding.

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ESTROGEN REPLACEMENT THERAPY USING MICRONIZED VAGINAL PROGESTERONE. G. Mezrow*, T. Koopersmith*, D. Shoupe, R.A. Lobo. Dept. of OB/GYN, USC School of Medicine, Los Angeles, CA 90033

Estrogen replacement therapy improves the quality of life for most postmenopausal women and decreases their risk of coronary heart disease and osteoporosis. A regimen with progestin is necessary if the women has a uterus to prevent the increased risk of endometrial hyperplasia and cancer seen with estrogen alone. Many women are intolerant to progestins and choose to discontinue therapy. Furthermore, progestins reverse the beneficial effects of estrogen on serum lipids. We previously showed that local release of progesterone (P) using a P releasing IUD was efficacious in preventing hyperplasia (NEJM 325:1811,1991). A randomized prospective trial was performed to determine if low dose micronized vaginal P given cyclically with estrogen can protect the endometrium while avoiding adverse systemic effects and irregular vaginal bleeding. We also wished to determine the ideal dose of micronized vaginal P to be used through pharmacokinetics studies, assessment of endometrial tissue levels and the evaluation of bleeding charts. Pretherapy testing included a pap smear, endometrial biopsy (EMB), ultrasound, FSH, total cholesterol, HDL cholesterol, and LDL cholesterol. Patients received conjugated equine estrogen .625mg daily throughout the trial and were randomized to receive one of three doses of micronized P (25mg, 50mg or 100mg) given for 14 days each month for six months. During the first month (day 7) of P patients had blood drawn prior to and 1, 2, 4, 8, and 24 hours after P administration. After three months patients had a repeat ultrasound, EMB and cholesterol panel. Patients kept a bleeding chart and record of side effects. All but one patient, who had very irregular bleeding, experienced light bleeding beginning between day 8 and 10 of P therapy for 4-8 days. None of the patients had any systemic side effects. All patients had an endometrial thickness ascertained by ultrasound after three months of therapy which was 5mm or less and all had EMB which were weakly proliferative. There was individual variation in time to maximal absorption with an average peak of 5 ± 1.08 hours. By 24 hours, serum P levels had returned to baseline. Maximum serum P after vaginal delivery ranged from 3.4-7.2 ng/ml. Endometrial P concentrations were variable but, were similar or greater than established luteal values. However, there was no correlation between these serum and endometrial levels and dose. Lipid profiles were not altered with therapy. We conclude that estrogen replacement with micronized vaginal P appears to be a safe alternative to oral progestin therapy which should result in better patient compliance due to the lack of systemic side effects.