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Natural progesterone, but not medroxyprogesterone acetate, enhances the beneficial effect of estrogen on exercise-induced myocardial ischemia in postmenopausal women.

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Abstract

OBJECTIVES:

We sought to compare the effects of estrogen/transvaginal progesterone gel with estrogen/medroxyprogesterone acetate (MPA) on exercise-induced myocardial ischemia in postmenopausal women with coronary artery disease or previous myocardial infarction, or both.

BACKGROUND:

Estrogen therapy beneficially affects exercise-induced myocardial ischemia in postmenopausal women; however, women with an intact uterus also take progestin to protect against uterine malignancies. The effects of combination estrogen/progestin therapy on myocardial ischemia are unknown.

METHODS:

Eighteen postmenopausal women (mean +/- SD age 59+/-7 years) were given 17-beta-estradiol in single-blinded manner for four weeks (1 mg/day for three weeks then 2 mg/day for one week). Estradiol (2 mg/day) was then continued, and the patients were randomized (double-blind) for 12 days to either transvaginal progesterone gel (90 mg on alternate days) and oral MPA placebo (10 mg/day), or vice versa. After another two weeks on estradiol alone, the patients crossed over to progestin treatment and repeated the protocol on the opposite treatment. Patients un-

derwent treadmill exercise testing after each estradiol phase and at day 10 of each progestin phase.

RESULTS:

Exercise time to myocardial ischemia increased after the first estrogen phase as compared with baseline (mean difference with 95% confidence interval [CI]: 72 s [34 to 110], $p = 0.001$), and was increased by combination estradiol/progesterone therapy as compared with estradiol/MPA therapy (92 s [35 to 149], $p = 0.001$). Two patients (11%) were withdrawn while taking estradiol/MPA owing to unstable angina.

CONCLUSIONS:

Combination estrogen/transvaginal progesterone gel increases exercise time to myocardial ischemia, as compared with estrogen/MPA. These results imply that the choice of progestin in women at higher cardiovascular risk requires careful consideration.