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Vasodilative potency induced with Estradiol in women with and without CAD during standardized stress:- two parallized, randomized, double-blind, placebo-controlled cross-over studies

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Objectives: Vasodilative effects of estrogens are thought to be the most important mechanism for getting cardiovascular protection during HRT The question should be answered if E2-induced blood-flow increasing effects also are working in women with coronary heart disease (CAD) compared to healthy women especially during physical stress. The rationale of this study was to establish a challenge test to assess the endothelial potency during physical stress.

Methods: Nitric oxide (NO), the strongest endogenous vasodilatator can be assessed by urinary sampling of cGMP. The main metabolite of serotonine, 5-hydroxyindole acetic acid (HIAA), can reflect platelet-endothelium interaction. cGMP and HIAA were assessed by EIA 2 hours before and 2 hours after symptom-limited bicycle exercise tolerance test ("ergometry"), which is a routinely used test to standardize physical stress.

Study Design and Patients: Two parallized, randomized, double-blind, placebo-controlled cross-over studies; study 1: 26 postmenopausal patients with coronary artery disease (CAD), diagnosed by coronary arteriography; study 2: 22 postmenopausal healthy women. Application of 4 mg sublingual estradiol (E2) or placebo 2 hours before ergometry. Cross-over-studies within 10 days.

Results: Regarding ECG and clinical symptoms no significant differences, with better performance (work-load, exercise time) in the healthy women. cGMP excretion increased in women with CAD after placebo by 60.6% (SEM 44.0) and after estradiol by 76.9% (SEM 22.1) compared to the value before the test. In healthy women cGMP increased after placebo by 40.3% (SEM 17.7) and after estradiol by 72.3% (SEM 22.0). In both groups only the increase during E2 was significant ($p<0.01$). Healthy women did produce about 3fold higher amounts of cGMP. No significant differences regarding HIAA-excretion with tendency of higher excretion in patients with CAD.

Conclusion: In healthy women the potency for E2-induced vasodilation is much higher compared to women with CAD. However, E2 can induce vasodilatation also in women with CAD if the endothelial potency is still high enough to produce NO. Our study-design could be used as standardized routine test to assess the individual endothelial reserve to produce enough vasodilatation even during physical stress which is the precondition for an effective cardiovascular protection during HRT. Serotonin-metabolite measurement seems not to be sensitive enough to predict platelet-endothelium interaction.

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