814 Coronary Vasomotor Tone in Different Patient Subsets

Wednesday, March 22, 1995, 4:00 p.m.–5:00 p.m.
Ernest N. Morial Convention Center, Room 22

4:00

814-1 Variations of Segmental Endothelium Dependent and Endothelium Independent Vasomotor Tone in the Long Term Follow Up After Cardiac Transplantation (Qualitative Changes in Endothelial Function)

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To assess segmental vasoconstrictor and dilator responses in patients after cardiac transplantation (CT) without obvious angiographic disease we infused the endothelium dependent vasodilator acetylcholine (ACH) and the endothelium independent vasodilator SIN-1 sequentially into the left coronary artery. ACH infusions always preceded SIN-1 infusions. Responses of 156 nonstenotic coronary segments (LAD and CX) were investigated in 26 patients (P). Group 1: 10 P 11.3 ± 3 months after CT. Group 2: 16 P 52 ± 11 months after CT. Five different responses to ACH followed by SIN-1 were observed: A) dilation followed by no change (fully preserved endothelium dependent function). B) dilation followed by further dilation. C) no change followed by dilation. D) constriction followed by dilation (defective endogenous NO-release and intact vascular smooth muscle function). E) constriction followed by constriction (defective endogenous NO-release and defective vascular smooth muscle function). *Results:* Different segmental reaction types in both groups.

	proximal LAD	distal LAD
Group 1:	20% A, 20% B, 30% C, 30% D	50% C, 50% D
Group 2:	19% C, 69% D, 12% E	12% C, 81% D, 7% E

Conclusion:(1) In only 20% of patients 1 year after CT the endothelium dependent vasodilation is completely preserved. In 40% of the patients 1 year after CT the endothelium shows segmental heterogeneity in response to ACH [absence of endothelium dependent vasodilation (type A and B) in the distal segment]. (2) In the long term course after CT more than 80% of P have defective endothelial function in proximal and distal segments [absence of endothelium dependent vasodilation (type A and B) in the proximal and distal segment]. Moreover approximately 10% have defective vascular smooth muscle function. Functional assessment of endothelial integrity in P after CT shows time dependent qualitative differences between proximal and distal coronary segments.

4:15

814-2 Responses of Internal Mammary Artery to Local Administration of Acetylcholine

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Internal mammary arteries (IMA) are widely used for coronary artery bypass grafting, and being reported to have a much higher long-term patency rate than that of saphenous veins. Therefore, we hypothesized that the endothelial function of IMA is better preserved compared with that of coronary arteries. To evaluate the endothelial function of IMA, acetylcholine (ACh) was selectively injected into IMA and both coronary arteries in 7 male and 4 female patients (mean age; 61 ± 11 (SD) years) with atypical chest pain and normal coronary arteriograms. Angiography was repeated before and after the selective injection of various doses of ACh and 1 mg of isosorbide dinitrate (ISDN). Injection of ACh into coronary arteries provoked neither chest pain nor ST-segment shifts. The diameter of IMA and both coronary arteries was measured with a computer-assisted analysis system. Arterial pressures and heart rates remained unchanged despite the selective injection of ACh and ISDN. Diameters (mm) were:

	Control	ACh			ISDN
		25 μg	50 μg	100 μg	
RCA	2.04 ± 0.49	1.87 ± 0.40**	1.62 ± 0.41**	–	2.44 ± 0.63**
LCA	2.06 ± 0.50	1.92 ± 0.50*	1.80 ± 0.49**	1.69 ± 0.46**	2.37 ± 0.54**
IMA	2.02 ± 0.53	2.22 ± 0.56**	2.36 ± 0.57**	–	2.43 ± 0.50**

*$p < 0.05$, **$p < 0.01$ vs. control values by ANOVA

The diameters of both coronary arteries were decreased by ACh in a dose-dependent manner, whereas IMA showed a dose-dependent dilation with ACh. These findings indicate that the endothelial function of IMA is well preserved, because ACh-induced endothelium-derived relaxing factors could counteract the contraction of vascular smooth muscle cells induced by ACh.

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814-3 Effect of Estradiol-17β upon Coronary Arterial Reactivity to Acetylcholine in Men with Coronary Artery Disease

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Estradiol-17β (E) has been shown to improve exercise-induced myocardial ischemia and reverse acetylcholine (ACh)-induced coronary constriction in female patients with coronary artery disease (CAD). To test this latter effect in men we studied the effect of intracoronary administration of E (2.5 μg) in 7 male patients with proven CAD (mean age 52 years). All patients underwent measurements of coronary artery diameter and coronary blood flow at rest, after control infusion and after infusion of ACh 1.6 and 16 μg per min, using quantitative angiography and intracoronary Doppler flowmetry. Infusions were performed before and 20 minutes after the intracoronary administration of E. Coronary artery diameter was similar after either control or estradiol-17β (mean ± SD; 2.9 ± 0.6 *vs* 2.8 ± 0.5 mm respectively, P = NS). E had no effect on the ACh-induced coronary constriction (ACh 1.6 μg per min; 2.7 ± 0.3 *vs* 2.7 ± 0.2 mm, P = NS; ACh 16 μg per min; 2.6 ± 0.3 *vs* 2.6 ± 0.3 mm, P = NS; post E *vs* pre E respectively). Likewise, E had no effect on basal coronary blood flow compared to control (77 ± 11 *vs* 75 ± 10 mL/min respectively, P = NS). E had no effect on the ACh-induced changes in coronary blood flow (ACh 1.6 μg per min; 95 ± 19 *vs* 90 ± 22 mL/min, P = NS; ACh 16 μg per min; 142 ± 27 *vs* 137 ± 39 mL/min, P = NS, post E *vs* pre E respectively).

Estradiol-17β does not appear to attenuate acetylcholine-induced coronary constriction nor enhance acetylcholine-induced coronary blood flow in male atherosclerotic coronary arteries *in vivo*. This is in contrast to the effect of estrogen in menopausal females. This suggests that the coronary vasculature reacts differently to estrogen in males and females.

4:45

814-4 Effect of Administration of Dehydroepiandrosterone on Cyclic-Guanidine-Monophosphate Plasma Levels in Men of Advancing Age

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Epidemiologic data suggest beneficial effects of dehydroepiandrosterone (DHEA) and dehydroepiandrosterone-sulfate (DS) in atherosclerosis and coronary artery disease. Aging is accompanied by a progressive decline in the secretion of DHEA and DS, paralleling that of growth hormone (GH) insulin like growth factor I (IGF-I) axis. Previous studies reported a significant increase of IGF-I serum levels after replacement therapy with DHEA in advancing age men and IGF-I has been shown to have a potent vasodilator effect in the forearm arterial blood flow in humans and the rat renal afferent microvasculature; an effect that can be blocked by inhibition of endothelial derived relaxing factor (EDRF), nitric oxide (NO). We investigated the effect of administration of DHEA on plasma levels of cyclic guanidine monophosphate (cGMP), the second messenger of NO activity and an indirect assay of NO release. We included 34 nonobese men, body mass index (BMI) 22–26 kg/m, age 47–74 years, normotensive and non insulin resistant in a double blind, placebo controlled, randomized study: 18 were treated with DHEA 150 mg daily for 12 days and 16 with placebo. DHEA increased from 3.7 ± 0.2 to 15.0 ± 1.4 μm/L ($p < 0.001$) in the DHEA group. No changes were observed in the placebo group. cGMP plasma levels increased from 3.22 ± 0.2 to 6.05 ± 0.21 Pmol/ml ($p < 0.005$) after administration of DHEA. In the placebo group no significant changes were observed. BMI, fasting insulin, serum lipids and blood pressure did not change during the study.

The increase of cGMP in the DHEA treated patients presumably occurs through increased NO production. We suspect that DHEA increases NO via IGF-I stimulation and this might be one of the mechanisms of the protective action of DHEA against coronary ischemic disease.