Effect of L-arginine on coronary endothelial function in cardiac transplant recipients. Relation to vessel wall morphology

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Abstract

Background

Coronary endothelial vasodilator dysfunction is a common finding in cardiac transplant recipients and may represent an early marker for the development of intimal thickening and graft atherosclerosis. The present study tested the hypothesis that endothelial dysfunction precedes intimal thickening and that administration of L-arginine, the precursor of endothelium-derived relaxing factor, improves endothelial vasodilator function of coronary conduit and resistance vessels if given at an early stage of graft atherosclerosis.

Methods and results

Acetylcholine (10(-6), 10(-5), 10(-4) mol/L) was infused into the left anterior descending or circumflex artery and repeated after intravenous infusion of L-arginine (10 mg.kg-1.min-1 over 20 minutes) in 18 cardiac transplant recipients. Epicardial responses were evaluated by quantitative angiography, and the microcirculation was studied by determination of coronary blood flow with a Doppler flow velocity wire. Intimal thickening was assessed by intravascular ultrasound (n = 14). In epicardial coronary arteries, acetylcholine tended to elicit vasoconstriction. Epicardial coronary vasoconstriction elicited by acetylcholine was attenuated by infusion of L-arginine (10(-4) mol/L, -6.8% versus -2.8%; P < .01); this beneficial effect was observed predominantly in patients with normal intravascular ultrasound characteristics. In coronary resistance vessels, acetylcholine induced vasodilation, reflected by increases in coronary blood flow. The acetylcholine-induced increase in blood flow was significantly enhanced with L-arginine (at a dose of 10(-4) mol/L, + 121% versus 176%; before versus after L-arginine, P < .002).

Conclusions

The coronary vasculature of cardiac transplant recipients exhibits a generalized endothelial dysfunction of conduit and resistance vessels. L-Arginine improves endothelial dysfunction of both coronary microvasculature and epicardial coronary arteries. The reversibility of epicardial endothelial dysfunction by L-arginine is more likely in vessels with normal wall morphology.