L-Arginine “Paradox” in Coronary Atherosclerosis

To the Editor:

Miner et al in a recent work used the steady-state $^{15}$N L-arginine to examine the transorgan L-arginine gradients in the peripheral and coronary circulation. They found that during acetylcholine infusion a significant gradient was detected, indicating that the stimulation of NOS induces arginine transport.

A body of evidence suggests that L-arginine supplementation improves endothelium-dependent vasomotor responses. This response to elevated extracellular L-arginine despite high intracellular L-arginine concentration has been called the “arginine paradox.”

We have examined the acute effects of intracoronary infusion of L-arginine in patients with stable angina and advanced atherosclerosis. L-Arginine administration was associated with significant dilatation of stenoses of proximal segments of both “normal” and diseased arteries, and of distal segments of diseased arteries ($P<0.01$). No significant changes were associated with D-arginine administration. The magnitude of dilatation of stenoses and all segments of both “normal” and diseased coronaries was greater after L-arginine ($P<0.05$), but not after D-arginine and substance P infusion, than it was after saline and substance P infusion. Administration of D- or L-arginine did not change the magnitude of substance P–induced dilatation. The dilation of proximal and distal segments in response to low-dose L-arginine was greater in patients with a serum cholesterol level ≤200 mg/dL than in patients with a level >200 mg/dL, whereas the response was the same in smokers and nonsmokers. During L-arginine infusion a larger proportion of complex stenoses than smooth stenoses dilated by >10%, and the magnitude of dilatation was greater at the site of complex stenoses ($P<0.05$). Our intracoronary studies indicate that acute intracoronary L-arginine supplementation may improve endothelium-dependent vasodilatation in coronary arteries in patients with coronary artery disease and support the theory of “arginine paradox.”

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