Endothelin Receptor Blockade in Congestive Heart Failure

To the Editor:

Of the many new therapeutic agents for slowing the progression of congestive heart failure (CHF), other than antagonizing the renin-angiotensin-aldosterone system, blocking the endothelin receptors seems to be most promising. The two latest reports published in Circulation1,2 render further support to this exciting concept.

Endothelin may contribute to the symptoms associated with CHF. Patients with the lowest exercise capacity, as measured objectively by maximum oxygen consumption (V̇O₂ max) were those who had the highest plasma levels of endothelin-1 at the time of maximal exercise.3 This finding suggests that endothelin may play a role in limiting the ability of the peripheral vasculature to dilate during exercise and, thus, contribute to exercise intolerance in these patients.4 Therefore, the reduced exercise capacity of patients with CHF may be more than a derangement in central hemodynamic variables, such as decreased cardiac output and increased pulmonary artery wedge pressure.

Several endothelin receptor antagonists have been developed. Tezosentan1 is being developed specifically for the short-term intravenous treatment of acute CHF. Studies with LU1352522 and bosentan5 indicate that short-term treatment with bolus intravenous or oral dosages is associated with improved systemic and pulmonary hemodynamic parameters. The short-term effects are encouraging, but these drugs are being developed to treat chronic CHF.1 Only long-term studies will determine whether the short-term effects translate into long-term benefit. Further, comparative trials with “standard” therapies for CHF, such as ACE inhibitors and β-blockers, are needed before these agents can be introduced into clinical use.

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