Drugs 2001; 61 (5): 628-629
0012-6667/01/0005-0628/$27.50/0

Levosimendan

A Viewpoint by Wilbert S. Aronow

Mount Sinai School of Medicine, New York, New York, USA

The therapy of congestive heart failure (CHF) depends on whether the left ventricular ejection fraction (LVEF) is abnormal or normal. The prevalence of normal LVEF associated with CHF increases with age, is higher in older women than in older men, and was 51% in 674 patients aged ≥60 years with CHF.[1] Patients with CHF and normal LVEF should not receive positive inotropic therapy. Phosphodiesterase (PDE) inhibitors such as milrinone,[2] flosequinan,[3] enoximone[4] and vesnarinone[5] have been demonstrated to increase mortality in patients with CHF and abnormal LVEF. No positive inotropic drug has been shown to reduce mortality in patients with CHF.

Levosimendan, a pyridazinone-dinitrile derivative, is a calcium sensitiser which also causes coronary and systemic vasodilation attributed to the activation of adenosine triphosphate-regulated potassium channels.

In a study involving 203 patients with severe low-output decompensated heart failure, 7 of 103 (6.8%) patients treated with intravenous (IV) levosimendan and 17 of 100 (17%) patients treated with dobutamine had worsening heart failure or died during the 24-hour infusion plus a 30-day follow-up period ($p = 0.039$).[6] In a study involving 504 patients with decompensated CHF after acute myocardial infarction, IV levosimendan administered for 6 hours was associated, during the first 24 hours, with a dose-related reduction in the combined incidence of worsening CHF or death (4% with levosimendan *vs* 8.8% with placebo; $p = 0.044$). At 14 days after treatment, overall mortality was lower in patients treated with levosimendan than in placebo recipients (11.4 *vs* 19.6%, $p = 0.029$).[7] These data are too preliminary to judge the efficacy of levosimendan in the treatment of CHF. Long term controlled clinical trials evaluating the effect of IV or oral levosimendan on cardiovascular morbidity and mortality in patients with stable or decompensated CHF are essential before one can evaluate fully the role of this drug in the treatment of patients with stable or decompensated CHF associated with abnormal LVEF. ▲

References

1. Aronow WS, Ahn C, Kronzon I. Comparison of incidences of congestive heart failure in older African-Americans, Hispanics, and whites. Am J Cardiol 1999; 84: 611-2
2. Packer M, Carver JR, Rodeheffer RJ, et al. Effect of oral milrinone on mortality in severe chronic heart failure: the PROMISE Study Research Group. N Engl J Med 1991; 325: 1468-75
3. Packer M, Rouleau J, Swedberg K, et al. Effect of flosequinan on survival in chronic heart failure: preliminary results of the PROFILE study [abstract]. Circulation 1993; 88 (Suppl. I): I-301
4. Uretsky BF, Jessup M, Konstam MA, et al. Multicenter trial of enoximone in patients with moderate to moderately severe congestive heart failure: lack of benefit compared with placebo. Circulation 1990; 82: 774-80
5. Cohn JN, Goldstein SO, Greenberg BH, et al. A dose-dependent increase in mortality with vesnarinone among patients with severe heart failure. N Engl J Med 1998; 339: 1810-6
6. Follath F, Cleland JGF, Just H, et al. Efficacy and safety of intravenous levosimendan in severe low-output heart failure [abstract no. 3406]. Circulation 1999 Nov; 100 (18 Suppl.): I-646
7. Nieminen MS, Moiseyev VS, Andrejevs N, et al. Randomized study on safety and effectiveness of levosimendan in patients with left ventricular failure after an acute myocardial infarct [abstract no. 3404]. Circulation 1999; 100 (18 Suppl.): I-646