Fifteen years of ACE-inhibition in congestive heart failure

Claudio Rapezzi

Institute of Cardiology, University of Bologna, Bologna, Italy

(Ital Heart J 2000; 1 (Suppl 3): S10-S11)

Address:

Dr. Claudio Rapezzi

Istituto di Cardiologia
Università degli Studi
Policlinico S. Orsola-Malpighi
Via Massarenti, 9
40138 Bologna

The activation of the renin-angiotensin system is one of the major consequences of reduced cardiac output in chronic congestive heart failure (CHF). Together with other mechanisms, this activation promotes myocardial dysfunction which further stimulates the renin-angiotensin system as well as the sympathetic nervous system.

During the last 15 years suppression of angiotensin Il formation by the inhibition of the angiotensin-converting enzyme (ACE) has produced exciting clinical results[1,2]. Several large scale clinical trials have documented that ACE-inhibitors reduce mortality and morbidity in patients with CHF. It is now clear that these results are obtained not only by the hemodynamic and myocardial action of ACE-inhibitors but also by their vascular effects. The inhibition of the renin-angiotensin system can beneficially alter some of the structural and functional changes seen in the arteries of patients with hypertension or CHF. This effect is largely independent of the ability of these agents to lower blood pressure. Furthermore, endothelial plasminogen activator inhibitor-1 production and secretion appear to be regulated by angiotensin II, while tissue-type plasminogen activator production and secretion are regulated by bradykinin[1]. Endothelial ACE is therefore strategically poised to regulate vascular fibrinolytic balance by virtue of its dual function in degrading bradykinin and converting angiotensin I to angiotensin II. These properties can explain the recently published results obtained in the HOPE trial[3]. It is now clear that ACE-inhibition can reduce death rate, myocardial infarction, and stroke in a broad range of high risk patients independently of the presence of low ejection fraction or heart failure.

From a clinical point of view it is important to underscore not only the advantages but also the adverse effects of ACE-inhibition and the limitations of their optimal use in the clinical area.

ACE-inhibitors may induce coughing as the result of bradykinin accumulation. Angioedema is a potentially life-threatening complication with an incidence of 0.1 to 0.2%. Renal dysfunction is a well-recognized complication which also may be partially mediated by bradykinin[4-6].

Indeed, despite the clear evidence that ACE-inhibitors improve survival, only about 30 to 50% of CHF patients in the community medical care setting actually receive these drugs.

High doses of ACE-inhibitors have been shown to be superior to low doses with respect to CHF symptoms, exercise performance and suppression of neurohumoral stimulation[3-6]. Despite this line of evidence, suboptimal dosage is a frequent problem in clinical practice. The most important reasons for nonprescription or underutilization of ACE-inhibitors appear to be lack of familiarity with the drug and concern about safety and adverse reactions, especially hypotension, renal failure and coughing.

AT_1 receptor antagonists can now be considered as a good alternative to ACE-inhibitors for patients unable to tolerate ACE-inhibitors.

References

1. Brunner-La Rocca HP, Vaddadi G, Esler MD. Recent insight into therapy of congestive heart failure: focus on ACE inhibition and angiotensin-II antagonism. J Am Coll Cardiol 1999; 33: 1163-73.
2. Packer M. Do angiotensin-converting enzyme

inhibitors prolong life in patients with heart failure treated in clinical practice? (editorial) J Am Coll Cardiol 1996; 28: 1323-7.
3. The Heart Outcomes Prevention Evaluation Study Investigators. Effects of an angiotensin-converting-enzyme inhibitor, ramipril, on cardiovascular events in high-risk patients. N Engl J Med 2000; 342: 145-53.
4. Roe CM, Motheral BR, Teitelbaum F, Rich MW. Angiotensin-converting enzyme inhibitor compliance and dosing among patients with heart failure. Am Heart J 1999; 138: 818-25.
5. Brunner-La Rocca HP, Weilenmann D, Kiowski W, Maly FE, Candinas R, Follath F. Within-patient comparison of effects of different dosages of enalapril on functional capacity and neurohormone levels in patients with chronic heart failure. Am Heart J 1999; 138: 654-62.
6. Philbin EF. Factors determining angiotensin-converting enzyme inhibitor underutilization in heart failure in a community setting. Clin Cardiol 1998; 21: 103-8.