Protection of the Cardiovascular System by Imidapril, a Versatile Angiotensin-Converting Enzyme Inhibitor

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Key words: Angiotensin-converting enzyme inhibitor—Cardiac hypertrophy—Heart failure—Hypertension—Imidapril—Myocardial ischemia—Renal insufficiency.

ABSTRACT

Imidapril hydrochloride (imidapril) is a long-acting, non-sulfhydryl angiotensin-converting enzyme (ACE) inhibitor, which has been used clinically in the treatment of hypertension, chronic congestive heart failure (CHF), acute myocardial infarction (AMI), and diabetic nephropathy. It has the unique advantage over other ACE inhibitors in causing a lower incidence of dry cough. After oral administration, imidapril is rapidly converted in the liver to its active metabolite imidaprilat. The plasma levels of imidaprilat gradually increase in proportion to the dose, and decline slowly. The time to reach the maximum plasma concentration (T_{max}) is 2.0 h for imidapril and 9.3 h for imidaprilat. The elimination half-lives (t_{1/2}) of imidapril and imidaprilat is 1.7 and 14.8 h, respectively. Imidapril and its metabolites are excreted chiefly in the urine. As an ACE inhibitor, imidaprilat is as potent as enalaprilat, an active metabolite of enalapril, and about twice as potent as captopril. In patients with hypertension, blood pressure was still decreased at 24 h after imidapril administration. The antihypertensive effect of imidapril was dose-dependent. The maximal reduction of blood pressure and plasma ACE was achieved with imidapril, 10 mg once daily, and the additional effect was not prominent with higher doses. When administered to patients with AMI, imidapril improved left ventricular ejection fraction and reduced plasma brain natriuretic peptide (BNP) levels. In patients with mild-to-moderate CHF [New York Heart Association (NYHA) functional class II–III], imidapril increased exercise time and physical working capacity and decreased plasma atrial natriuretic peptide (ANP) and BNP levels in a dose-related manner. In patients with diabetic nephropathy, imidapril decreased urinary albumin excretion. Interestingly, imidapril improved asymptomatic dysphagia in patients with a history of stroke. In the same patients it increased serum substance P levels, while the angiotensin II receptor antagonist losartan was ineffective. These studies indicate that imidapril is a versatile ACE inhibitor. In addition to its effectiveness in the treatment of hypertension, CHF, and AMI, imidapril has beneficial effects in the treatment of diabetic nephropathy and asymptomatic dysphagia.
Good tissue penetration and inhibition of tissue ACE by imidapril contributes to its effectiveness in preventing cardiovascular complications of hypertension. The major advantages of imidapril are its activity in the treatment of various cardiovascular diseases and lower incidence of cough compared with some of the older ACE inhibitors.