Reduction of Renal Function by Angiotensin-Converting Enzyme Inhibitors: Effect of Verapamil

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Dear Sir,

There is a large corpus of papers claiming a beneficial effect of ACEI in renal function in hypertensive patients, particularly in diabetic hypertensives [1]. A recent meta regression analysis of 100 clinical trials in patients with IDDM and NIDDM suggests that ACEI exhibits a specific renoprotective effect independent of the antihypertensive effect [2]. There are studies giving evidence that ACEI (lisinopril) and non-dihydropyridine calcium channel blockers are superior in lowering blood pressure, albuminuria, and reducing the rate of decline of GFR than the combination of diuretics and beta-blockers [3]. Enalapril is more effective than atenolol in preserving GFR in spite of a similar reduction in blood pressure and urinary albumin excretion [4]. On the other hand, a worsening of renal function in some patients treated by ACEI has recently been communicated [5], particularly in patients with some degree of renal deterioration. Until now this side effect has been overcome by discontinuation of ACEI [5]. We present data concerning the influence of ACEI on serum creatinine in 11 patients aged 68.45 ± 1.46 years (range 23-82), 5 females and 6 males with mean serum creatinine before ACEI of $110.5 \pm 41.5 \mu\text{mol/L}$. In a period of 5.87 ± 0.51 months the serum creatinine was raised to $396.03 \pm 25.6 \mu\text{mol/L}$, ($p < 0.05$). ACEI were withdrawn and serum creatinine reverted towards values previous to ACEI treatment ($120.22 \pm 41.5 \mu\text{mol/L}$). Thus, we confirm the data of Gotloib et al. [5] suggesting that ACEI can induce renal failure in some hypertensive patients, and that this effect can be reverted by discontinuation of ACEI. However, if ACEI are discontinued, the possible beneficial effects of these drugs on renal function are also eliminated.

Because of this, the aim of the present paper is to show the effect of adding nondihydropyridine calcium channel blockers while maintaining the same dose of ACEI instead of withdrawing it in patients in whom serum creatinine increases with ACEI treatment. We have performed this study in 4 patients. The first patient is a 68-year-old woman with IDDM and serum creatinine $294.37 \mu\text{mol/L}$, BP 200/80 mm Hg and urinary albumin excretion (UAE) 1.05 g/day . She started on enalapril 10 mg b.i.d. to control BP and to reduce proteinuria. After 18 days serum creatinine raised to $381.89 \mu\text{mol/L}$, with a BP of 170/75 mm Hg. Maintaining the same dose of enalapril, verapamil at a dose of 80 mg b.i.d. was introduced. Seven days later serum creatinine was 327.97

$\mu\text{mol H}$ and BP 170/70 mm Hg. Two weeks later serum creatinine was 309.40 $\mu\text{mol l}^{-1}$, BP 160/60 mm Hg, and UAE 1.4 g/day. One month later serum creatinine was 303.21 $\mu\text{mol H}$, BP 155/80 mm Hg. Four months later under the same treatment serum creatinine was 318.24 $\mu\text{mol l}^{-1}$, BP 160/75 mm Hg and UAE 0.35 g/day. Eight months later verapamil was discontinued remaining in 10 mg of enalapril. Under these conditions, creatinine was raised to 369.51 $\mu\text{mol H}$, with a BP of 140/80 mm Hg and UAE 2.03 g/day.

The second patient was a 67-year-old man referred to us because of uncontrolled blood pressure in spite of treatment with beta-blockers, diuretics and alpha-methyl-

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pa. BP was 180/102 mm Hg and serum creatinine 100.77 $\mu\text{mol H}$. He was started on lisinopril 5 mg/day, which was later raised to 5 mg b.i.d. Three months later serum creatinine was 132.6 $\mu\text{mol l}^{-1}$, and BP 165/95 mm Hg. Verapamil at a dose of 80 mg b.i.d. was prescribed. Nine months later serum creatinine was 103.42 $\mu\text{mol H}$ and BP 165/86 mm Hg.

The third patient was a 74-year-old woman with NIDDM and serum creatinine 183.87 $\mu\text{mol H}$, BP 180/95 mm Hg and UAE 1.68 g/day. She was started on lisinopril 5 mg t.i.d. and then changed to enalapril 10 b.i.d. and two diuretics. She was referred to us 7 months later with a serum creatinine of 321.78 $\mu\text{mol H}$, BP 160/90 and UAE 2.576 g/day. Enalapril at a dose of 10 mg b.i.d., that was not changed, and verapamil at a dose of 80 mg b.i.d. were prescribed. One week later serum creatinine was 229.84 $\mu\text{mol H}$, and BP 160/90. Two weeks later serum creatinine was 212.16 $\mu\text{mol H}$ and BP 140/90. Three weeks later serum creatinine was 212.16 $\mu\text{mol l}^{-1}$, BP 140/90 mm Hg and UAE 2.786.

The fourth patient was a 35-year-old woman with high blood pressure secondary to renal polycystic kidney disease. BP was in the range of 140-130/95-80 mm Hg, serum creatinine 114.92 $\mu\text{mol H}$, endogenous creatinine clearance 45 ml min⁻¹. She was started on enalapril 10 mg b.i.d. Three weeks later creatinine was 139.67 $\mu\text{mol H}$ and BP of 125/85 mm Hg. Verapamil at a dose of 80 mg b.i.d. was prescribed. Four weeks later creatinine was 114.92 $\mu\text{mol H}$, endogenous creatinine clearance 77 ml min⁻¹ and BP of 127/84 mm Hg.

From the above observations, we conclude that by adding verapamil instead of discontinuing ACEI, it is possible to reverse the increase in serum creatinine induced by ACEI in patients in whom ACEI are indicated.

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