Severe Reduction of Renal Function in Hypertensives and/or Diabetics Induced by Angiotensin-Converting Enzyme Inhibitors

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Dear Sir,

Some clinical studies postulated that angiotensin-converting enzyme inhibitors (ACEI) alone or in combination with diuretics have a renal protective effect in hypertensive patients with either moderately or severely impaired renal function [1] as well as in insulin-dependent diabetics with ne-phropathy [2]. Even though some investigators reported detrimental effects of ACEI upon renal function in diabetics [3] and in patients with serum creatinine levels > 1.5 mg/dl [4], other authors postulated that these drugs can be safely administered in both clinical situations [5].

The purpose of this report is to present 14 patients referred to our clinic because of mild to severe renal failure which developed within approximately 10 weeks after starting therapy with ACEI. The observations were made on 10 male and 4 female patients with a mean age of 68.21 ± 12.09 years, all of them with a history of arterial hypertension for a mean period of 14 ± 9 years; 6 patients also suffered from insulin-dependent diabetes for long periods of time (mean 23 ± 8 years).

The patients showed high mean serum creatinine levels (table 1), and even though the blood pressure was effectively controlled (table 1) by using different combinations of drugs like α -methyl dopa, prazosin hydro-chloride, nifedipine, and β -blockers with thiazides, this therapy was changed to ACEI, the main goal being to delay the deterioration of the kidney function.

The mean dosage of captopril was 41.07 ± 20.04 (range 12.5-75) mg/day in 7 patients, whereas that of enalapril was 18.60 ± 10.30 (range 10-40) mg/day in the other 7. Diuretics (thiazides or furosemide) were prescribed to all patients. This therapy was maintained for periods ranging from 2 to 10 (mean $\pm$ SD 3.4 ± 0.9) weeks, when patients were referred to our clinic because of significantly higher levels of serum creatinine (table 1). Hyperkalemia was detected in 10 cases. Dialysis was started in 2 patients. One of them had a partial recovery of the renal function (serum creatinine $398 \mu\text{mol/l}$), whereas the other one started CAPD. Three months after interrupting ACEI, the mean serum creatinine levels remained significantly higher than those observed when using the other antihypertensive drugs. The blood pressure did not significantly change with either therapeutic approach (table 1).

An extensive review of this topic [6] suggested that a retarding effect of ACEI on the progression of chronic, nondiabetic human renal failure, as postulated by other groups [1, 2], is far from being clearly demonstrated. Conversely, in another study performed in diabetics [2], it was claimed that captopril delayed the progression of renal failure, even though the percentages of patients needing renal replacement therapy at the end of the observation period in both placebo (15.34%) and captopril (9.66%) groups were not significantly different ($p = 0.11$, two-tailed chi-square test with the Yates correction; 95% confidence interval -0.006, < 0.05, < 0.12 NS). So far, these considerations, in addition to our disappointing observations, suggest

Table 1. Mean serum creatinine and blood pressure values before and after ACEI treatment

Serum creatinine, $\mu\text{mol/l}$

227.19 ± 95.47 644.44 ± 150.28 376.58 ± 184.76 A vs. B < 0.001

A vs. C < 0.05 B vs. C < 0.001

Systolic blood pressure, mm Hg

161.11 ± 5

153 ± 13.0

$161. \pm 9.0$

A vs. B NS

A vs. C NS

Diastolic blood pressure, mm Hg

87 ± 5.4

82 ± 6.0

85 ± 6.0

B vs. C NS

Analysis was performed using the two-tailed Bonferroni method with multiple comparisons. that the beneficial effects of ACEI in delaying the progression of kidney dysfunction have not yet been proved and that their use in diabetic or nondiabetic patients with chronic renal disease carries the risk of precipitating further renal deterioration.

References

- Praga M, Hernandez E, Montoyo C, Andres A, Rullope LM, Rodicio JL: Long-term beneficial effects of angiotensin-converting enzyme inhibition in patients with nephrotic proteinuria. *Am J Kidney Dis* 1992;20:240-248.
- Lewis EJ, Hunsicker LG, Bain RP, Rohde RD (for the Collaborative Study Group): The effect of angiotensin-converting enzyme inhibition on diabetic nephropathy. *N Engl J Med* 1993; 329:1456-1462.
- Packer M, Lee WH, Medina N, Yushak N, Kerssler PD, Gottlieb SS: Influence of diabetes mellitus on changes in left ventricular performance and renal function produced by converting enzyme inhibition in patients with severe chronic heart failure. *Am J Med* 1987;82: 1119-1126.
- Jenkins AC, Dreslinski GR, Tadross SS, Gogel JF, Fand R, Herczeg SA: Captopril in hypertension: Seven years later. *J Cardiovasc Pharmacol* 1985;7(suppl 1):96-101.
- Bjork S, Nyberg G, Mulec H, Granerus G, Heritz H, Avrell M: Beneficial effects of angio-tensin converting enzyme inhibition on renal function in patients with diabetic nephropathy. *Br Med J*

1986;293:467-470. Wee PM, Epstein M: Angiotensin-converting enzyme inhibitors and progression of non-diabetic chronic renal disease. Arch Intern Med 1993;153:1749-1759.
231