Angiotensin-Converting Enzyme Inhibitors in Diabetics with Hypertension -A Cautionary Note

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Dear Sir,

Angiotensin converting enzyme (ACE) inhibitors are currently considered to be valuable anti-hypertensive agents in the treatment of hypertension associated with diabetes mellitus. The renal lesion of diabetes is associated with increased intraglomerular pressure which is reduced by these drugs, reducing the proteinuria and possibly protecting against the subsequent development of glomerular structural injury [1–3]. We report 2 cases of renal failure induced by ACE inhibitors in 2 elderly hypertensive diabetic patients which again draws attention to a potential problem associated with the use of these drugs.

Case Reports

Case 1

A 64-year-old woman with hypertension for 20 years and non-insulin-dependent diabetes for 5 years, developed poor blood pressure control in January 1988 with figures averaging 180/120 mm Hg on atenolol and nifedipine retard therapy. Her blood glucose control was satisfactory on glipizide 10 mg twice a day. At this time her plasma urea was 12.5 mmol/l (75 mg/dl) and creatinine 167 μ mol/l (1.8 mg/dl). Urine showed + protein (0.6 g/24 h). To improve blood pressure control, enalapril 20 mg daily was commenced in June 1988. She was referred with deteriorating renal function in October 1988 with a plasma urea of 18 mmol/l (108 mg/dl) and creatinine of 380 μ mol/l (4.1 mg/dl), some 5 months after starting enalapril therapy. Blood pressure was 210/90 mm Hg in the right arm and 130/90 mm Hg in the left arm. Grade II hypertensive retinopathy was recorded. Bilateral carotid bruits were noted with a reduced left femoral pulse and absent distal pulses in the left leg. Because of the suspicion of renal artery stenosis, a renal arteriogram was performed which showed that each kidney had a double blood supply, but the cephalad artery of the left kidney was totally occluded while the artery to the lower pole was stenosed at its origin. The caudal artery on the right was totally occluded while the upper pole artery was tightly stenosed at its origin. The lesion was not considered appropriate for angioplasty. Enalapril was stopped and her renal function improved and subsequently remained stable with a plasma urea of 13 mmol/l (78 mg/dl) and creatinine of 254 μ mol/l (2.8 mg/dl) when last seen in November 1988.

Case 2

A 57-year-old woman with non-insulin-dependent diabetes of 8 years known duration, on gliclazide 16 mg twice a day was first noted to be hypertensive in November 1987 and commenced on nifedipine and frusemide. In December 1987, plasma urea was 19 mmol/l and

creatinine 170 $\mu\text{mol/l}$ with + + + proteinuria on labstix testing (not quantitated). Captopril in a dose of 12.5 mg twice a day was added in May 1988 for better blood pressure control. In November 1988 she was referred with acute on chronic renal failure. At this time, blood pressure was 200/95 mm Hg and she had signs of fluid overload. Her plasma urea was 60 mmol/l (360 mg/dl) and creatinine 1,416 $\mu\text{mol/l}$ (15.6 mg/dl). A Mag III isotope renogram showed very poor definition of the right and left kidneys. Both kidneys showed no significant function or evidence of renal blood flow. Ultrasound showed a small smooth left kidney (8.5 cm), the right kidney was of normal size (12.8 cm). There was no evidence of obstruction. This patient commenced haemodialysis and has remained dialysis dependent.

Comments

It is well known that diabetes mellitus is associated in the long term with an increased incidence of arteriosclerosis. It is highly likely that both these diabetic patients had advanced renovascular disease at the time of commencement of ACE inhibitor treatment. It has been suggested that when renal perfusion is reduced because of renal artery stenosis, angiotensin-II-dependent efferent arteriolar constriction maintains glomerular filtration rate by increasing glomerular capillary pressure. In such circumstances, ACE inhibitors would impair this protec-

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tive mechanism by preventing AngII generation and subsequent efferent arteriolar constriction. The resulting fall in glomerular capillary pressure will cause a decrease in glomerular filtration rate [4, 5]. Our first patient developed reversible renal insufficiency which has been described in hypertensive patients with bilateral renovascular disease [4,5]. The second patient developed an irreversible renal insufficiency which we attribute to renal artery occlusion in a patient with a single functioning kidney.

Caution is required with the use of ACE inhibitors in long-term or elderly diabetic patients. Their use in such patients with co-existing renovascular disease may precipitate irreversible renal failure.

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