Acute renal failure with ACE inhibition in aortic coarctation

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Summary: A 43 year old man with inoperable aortic coarctation and severe hypertension requiring near maximal anti-hypertensive treatment was admitted in severe heart failure. After 2 weeks of treatment the heart failure and blood pressure were incompletely controlled and angiotensin converting enzyme (ACE) inhibitor was started. Serum creatinine was normal before starting the ACE inhibitor and on discharge from hospital. The patient was re-admitted a week later with gross fluid retention and in renal failure. In the absence of alternative causes, a diagnosis of ACE inhibitor-induced renal failure was made and treatment was stopped. The patient required haemodialysis for 2 days and within 1 week the renal function had reverted to normal and has remained so for 1 year. We propose that the renal haemodynamics in severe aortic coarctation are similar to those in bilateral severe renal artery stenosis and advise caution in the use of ACE inhibitors for adults with aortic coarctation.

Introduction

Angiotensin-converting enzyme (ACE) inhibitors now have a prominent role in managing heart failure and hypertension. They are generally well tolerated and safe, but infrequently cause renal failure[1] typically in patients with bilateral severe renal artery stenosis[2] or stenosis of the artery serving a single functioning kidney.[2,3] We report a patient with aortic coarctation who developed reversible acute renal failure after starting ACE inhibitor treatment, and suggest that ACE inhibitors should be used with caution in severe coarctation.

Case report

A 43 year old male construction worker known to have inoperable aortic coarctation and severe hypertension was admitted in 1991 with uncontrolled left ventricular failure. Hypertension and clinical features of coarctation had been discovered 19 years before, when aged 25, at a routine examination for employment. Arteriography confirmed a tight 'shelf-like' coarctation at an unusually distal position at the level of T12. Surgical exploration at that time confirmed the tight coarctation at the level of T12 with a length of approx-

imately 4 cm. An attempt at repair had to be abandoned because of numerous very large thin-walled collateral vessels, and he was managed medically. Blood pressure control proved difficult, with readings often > 200/110 mmHg until the introduction of minoxidil and frusemide 11 years before admission. Thereafter blood pressure averaged 164/90 mmHg while taking atenolol 50 mg, hydralazine 200 mg, minoxidil 40 mg and frusemide 160 mg daily. He had severe left ventricular hypertrophy but remained symptom-free until 3 years before admission, when he developed atrial fibrillation and mild cardiac failure. The latter was controlled by increasing the dose of frusemide to 250 mg daily. He was reassessed for possible surgical treatment but the risk was considered prohibitive. Throughout this time renal function remained normal with serum creatinine averaging 95 μmol/l.

When admitted he had had 2 weeks of increasing exertional dyspnoea, orthopnoea, paroxysmal nocturnal dyspnoea and oedema. Examination revealed disproportionate muscle development of the upper body, atrial fibrillation at 110/minute, blood pressure of 162/98 mmHg, peripheral oedema, widespread prominent superficial collaterals, displaced thrusting apex beat, a long loud precordial systolic murmur and femoral pulses, which were readily palpable and slightly delayed. An electrocardiogram (ECG) showed atrial fibrillation and severe left ventricular hypertrophy, a chest X-ray showed cardiomegaly, rib notching and pulmonary

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oedema, and an echocardiogram severe concentric left ventricular hypertropy with normal valves. Serum creatinine was 100 μmol/l. He was treated initially by stopping atenolol, adding digoxin and amiloride, and increasing the dose of frusemide to 500 mg daily. After 12 days his heart failure was incompletely controlled and the blood pressure was still high (average 175/105 mmHg), and ACE inhibitor treatment was introduced. Amiloride was stopped, frusemide was omitted temporarily and an initial dose of captopril 6.25 mg was given without ill-effect, and particularly without hypotension. Treatment was continued with enalapril and he was discharged 3 days later taking enalapril 5 mg daily with frusemide 500 mg, minoxidil and digoxin. Serum creatinine was normal before starting the ACE inhibitor (70 μmol/l) and on discharge 3 days later (74 μmol/l).

He was re-admitted 6 days after discharge with gross fluid retention. He was virtually anuric for 24 hours and now had serum creatinine of 805 μmol/l, urea 48.6 mmol/l, sodium 129 mmol/l, potassium 5.4 mmol/l and bicarbonate 18 mmol/l. Urine showed trace proteinuria but no blood, cells or casts. Blood pressure was 174/70 mmHg. In the absence of alternative causes, a presumptive diagnosis of acute renal failure caused by ACE inhibitor treatment was made and enalapril was stopped. He required haemodialysis for 2 days (Figure 1) but had a prompt diuresis, with urine output on successive days 1.6, 5.5 and 6.7 litres. His serum creatinine returned to normal within 1 week (Figure 1). Other than the ACE inhibitor, all drugs

taken previously were reintroduced, and renal function has remained normal (Figure 1) even when the dose of frusemide was subsequently increased to 1,000 mg daily.

Discussion

The acute renal failure was ascribed to ACE inhibitor treatment because of the close temporal relationship, the rapid and complete recovery after enalapril was withdrawn and the absence of any other recognized cause of acute renal failure. At no time did he have hypotension or volume depletion, which might precipitate acute renal failure. ACE inhibitors have rarely precipitated renal failure in patients with pre-existing renoparenchymal disease,[4] prolonged severe diarrhoea,[1] or concomitant use of non-steroidal anti-inflammatory drugs,[1] but none of these circumstances were present. We propose that the renal haemodynamics in this patient with severe aortic coarctation resembled those of bilateral severe renal artery stenosis and that the acute renal failure had a mechanism similar to the renal failure induced by ACE inhibitors in critical renovascular disease.[5] In health the renal blood flow and glomerular filtration rate remain relatively constant when mean arterial pressure varies over a wide range. This autoregulation is effected by changes in preglomerular resistance and by the arteriole leading from the glomerulus–efferent arteriolar resistance. Normally renal blood flow is kept constant largely by changes in
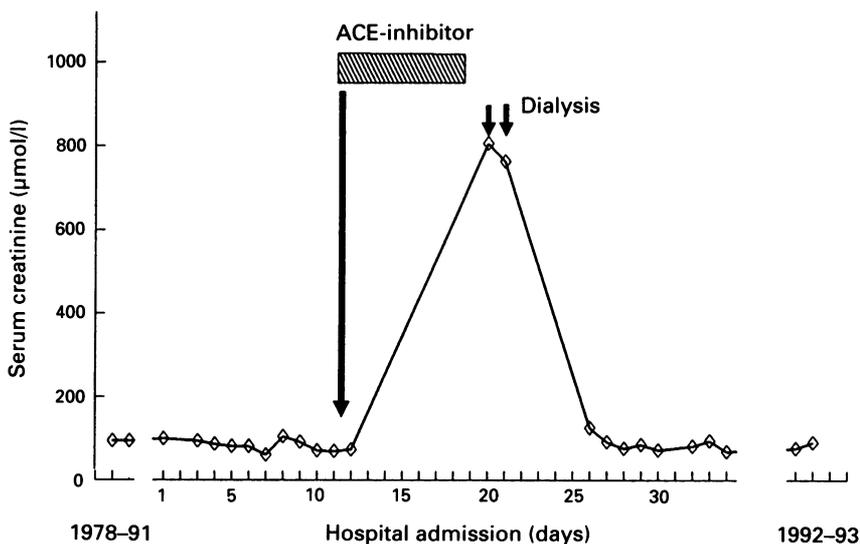

Figure 1 Changes in serum creatinine concentration related to angiotensin converting enzyme (ACE) inhibitor therapy.

preglomerular resistance rather than at the efferent arteriolar level. However, at the lower end of the autoregulatory range, preglomerular resistance is minimal and glomerular filtration rate then depends on an increase in efferent arteriolar resistance. This increase in postglomerular resistance is mediated by a direct intrarenal effect of angiotensin II, and renal perfusion and glomerular filtration are thus critically dependent upon angiotensin II.[5] In this situation ACE inhibition decreases postglomerular resistance with consequent reduction or even cessation of glomerular filtration.[5] This is the mechanism of the renal failure, which occurs with ACE inhibitor therapy in a significant proportion of patients with bilateral severe renal artery stenosis[2] or stenosis of the artery to a solitary functioning kidney.[2,3]

In the low pressure system distal to an aortic coarctation, we propose that in some cases renal autoregulation may be in the range where it is dependent on angiotensin II-induced efferent arteriolar constriction. There is evidence from both animal and human studies that the renin angiotensin system is activated in coarctation,[6-9] presumably as a renal protective mechanism. In this patient the atypical site and the length of the coarctation, starting at T12 and extending for 4 cm, may have resulted in the coarct involving the renal arteries and thus influencing renal haemodynamics directly. Patients with severe and atypical coarctation may therefore be at risk of developing renal failure with ACE inhibitor therapy as occurred in this case. ACE inhibitors have been used with variable success to control blood pressure in patients with coarctation as a temporary measure to prepare infants with cardiac failure for corrective surgery.[10-12] Renal failure has not been reported but nevertheless we advise caution in the use of ACE inhibitors for adult patients with severe coarctation of the aorta.

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