Reversible impairment of renal function associated with enalapril in a diabetic patient

Education

Éducation

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This article has been peer reviewed.

CMAJ 1998;159:1279-81

Abstract

ACUTE RENAL FAILURE AND HYPERKALEMIA due to angiotensin-converting enzyme inhibitors have been described in diabetic patients with other predisposing conditions. The case reported here involves a patient with type 1 diabetes mellitus, microalbuminuria and normal renal function who was treated with enalapril. Two years after initiation of this therapy, at a time when glycemic control was poor, he presented with symptomatic hyperkalemia and impaired renal function accompanied by hyporeninemic hypoaldosteronism. This case illustrates that reversible impairment of renal function and hyperkalemia can present after 2 years of treatment with angiotensin-converting enzyme inhibitors in patients with precipitating factors.

Résumé

ON A DÉCRIT DES CAS D'INSUFFISANCE RÉNALE AIGUË ET D'HYPERKALIÉMIE attribuable aux inhibiteurs de l'enzyme de conversion de l'angiotensine chez des patients diabétiques atteints d'autres affections prédisposantes. Le rapport d'étude de cas porte sur un patient atteint de diabète sucré de type 1 et de microalbuminurie, qui avait une fonction rénale normale et qui prenait de l'énalapril. Deux ans après le début du traitement, au moment où sa glycémie était mal contrôlée, il a présenté des symptômes d'hyperkaliémie et de déficience de la fonction rénale, conjugués à un hypoaldostéronisme hyporéninémique. Ce cas démontre la présence possible d'une déficience réversible de la fonction rénale et d'une hyperkaliémie après deux ans de traitement aux inhibiteurs de l'enzyme de conversion de l'angiotensine chez des patients qui ont des facteurs précipitants.

Angiotensin-converting enzyme (ACE) inhibitors are used to treat hypertension, heart failure and diabetic nephropathy. Acute renal failure due to ACE inhibitors has been described in patients with bilateral renal artery stenosis, with a single kidney and unilateral stenosis, with renal disease, and with severe congestive heart failure and concomitant diuretic therapy and in renal transplant recipients.[1–4] After ACE inhibitors are discontinued, renal function usually returns, although exceptions have been reported.[5] ACE inhibitors can also induce hyperkalemia, especially in patients with cardiac failure or diabetes mellitus, in those on a low-salt diet and those taking potassium-sparing diuretics or nonsteroidal anti-inflammatory agents.[6,7]

Case report

A 31-year-old man with insulin-dependent diabetes mellitus presented with a 2-week history of paresthesias, tingling and leg weakness associated with poor glycemic control. He had had diabetes for 18 years. In recent years his metabolic control had usually been poor (glycosylated hemoglobin greater than 8.0%, normally less than 5.8%). He had proliferative retinopathy and sudomotor dysfunction. Hypertension and incipient diabetic nephropathy had been diagnosed at another centre 2 and 4 years earlier. Enalapril (5 mg/day) had been initiated after the most recent evaluation and during the subsequent 2 years he had done well. He was not

taking any medication other than insulin and enalapril. The patient's blood pressure was 120/85 mm Hg and his serum chemistry was as follows: potassium 6.3 (normally 3.9–5.1) mmol/L, sodium 132 (normally 140–148) mmol/L, glucose 31.1 (normally 4.1–6.4) mmol/L, urea 9.4 (normally 3.1–7.4) mmol/L, creatinine 148 (normally 68–114) μmol/L and urinary excretion of albumin 57.3 (normally less than 20) μg/min (i.e., microalbuminuria). Glycosylated hemoglobin was 8.7% and urine was negative for ketone bodies; blood pH was not determined.

The patient was admitted to the endocrinology ward, where the enalapril was discontinued and calcium polystyrene sulfonate (10 g every 12 hours) was initiated. He was discharged after 1 week. His glycemic control and indicators of renal function improved steadily and after 2 months were within the normal ranges (Table 1). His blood pressure at follow-up was consistently above 140/90 mm Hg, and therapy with α-methyldopa was initiated. Renal ultrasonography showed that the kidneys were of normal size (12 and 11.5 cm in length) without any morphologic abnormality. Neither echodoppler imaging of the renal arteries nor captopril renography suggested reno-vascular disease. The patient's sodium intake was not restricted, and 4 months after the enalapril treatment was discontinued his plasma renin activity and aldosterone level in the supine and upright positions indicated hyporeninemic hypoaldosteronism: plasma renin activity, supine < 0.3 (normally 0.4–4.0) $\mu g \cdot L^{-1} \cdot h^{-1}$ and upright 0.57 (normally 1.5–10.0) $\mu g \cdot L^{-1} \cdot h^{-1}$; aldosterone, supine 132.5 (normally 220–570) pmol/L and upright 216.1 (normally 300–1000) pmol/L. Plasma cortisol and cortisoluria levels were normal.

Comments

We have described a patient with type 1 diabetes mellitus and diabetic nephropathy who presented with impaired renal function and disproportionate hyperkalemia after being treated with ACE inhibitors. Renal function recovered gradually after the enalapril therapy was discontinued and glycemic control improved. However, the recovery period was too long to attribute the improvement solely to hyperglycemia-induced volume depletion. Hricik[8] has suggested that volume depletion is an important mechanism in captopril-induced renal insufficiency, and McMurray and Matthews[9] described 3 patients receiving ACE inhibitors in whom acute renal failure developed after intercurrent gastrointestinal fluid losses. We attribute the renal-function impairment in this patient to both volume depletion and enalapril therapy. Poor metabolic control in the weeks before presentation caused volume depletion, as manifested by the low-normal blood pressure at presentation. In hypovolemia, aldosterone is required to maintain blood volume and angiotensin II to maintain arterial tone and glomerular filtration rate. We suggest that the blocking of these compensatory mechanisms by enalapril made the patient more prone to renal failure. It is remarkable that 2 months after presentation, baseline renal function had returned to normal; renal failure induced by ACE inhibitors is more common in patients with known renal failure.[4,5,9,10]

In this patient the hyperkalemia was probably multifactorial in origin, but latent hyporeninemic hypoaldosteronism and ACE inhibitor therapy were probably the important predisposing factors. Hyporeninemic hypoaldosteronism is characteristic of diabetic patients with mild to moderate renal failure. Most patients are asymptomatic, and salt-wasting is infrequent because plasma aldosterone levels are usually sufficient to maintain normal sodium balance.[11] Isolated hyporeninemic hypoaldosteronism does not usually lead to hyperkalemia,[12] except when there is concomitant impairment of renal function.[12,13] It is possible that there was a progressive development of the hyporeninemic hypoaldosteronism; however,

Table 1: Indicators of renal function at presentation and follow-up

Time of measurement	Indicator*					
	Sodium, mmol/L	Potassium, mmol/L	Chloride, mmol/L	Urea, mmol/L	Creatinine, μmol/L	Urinary excretion of albumin,† μg/min
At presentation	132	6.3	103	9.4	148	57.3
After presentation						
1 wk	130	5.4	96	10.9	116	223.0
3 wk	140	5.0	108	6.6	117	ND
7 wk	134	4.2	97	6.5	114	70.4
8 wk	138	4.2	102	4.4	107	ND
Normal range	140–148	3.9–5.1	96–109	3.1–7.4	68–114	< 20

Note: ND = not determined. At the time of presentation, the patient had been taking enalapril (5 mg/day) for 2 years. After presentation, the enalapril was discontinued, and calcium polystyrene sulfonate (10 g every 12 hours) was initiated. After 7 weeks, this treatment was discontinued, such that the patient was taking no medication at 8 weeks.
*For serum, except where otherwise indicated.
†Rate of excretion 20 μg/min or higher indicates microalbuminuria (i.e., incipient nephropathy).

the patient was asymptomatic during the 2 years he was receiving ACE inhibitor therapy. Symptomatic hyperkalemia developed only when glycemic control was poor.[14] We suggest that hyperglycemia may have triggered the hyperkalemia, through hyperglycemia-induced release of potassium from the cells when renal function was impaired.[15] The contribution of the ACE inhibitor was probably significant, because the patient has reported similar episodes of hyperglycemia at follow-up, and potassium levels have remained within the upper-normal range.

ACE inhibitors have been recommended as first-line antihypertensive drugs for diabetic patients with nephropathy. Plasma potassium and creatinine levels should be measured shortly after the therapy is initiated.[3,7] This case illustrates that impaired renal function and hyperkalemia can present as late as 2 years after ACE inhibitor treatment when precipitating factors are present.

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