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LETTER TO THE EDITOR

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Lithium intoxication in an elderly patient after combined treatment with losartan

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Angiotensin-1-converting enzyme (ACE) inhibitors decrease lithium clearance through increased natriuresis [1]. Losartan is a non-peptide-specific angiotensin 2 receptor (AT2 receptor)-antagonist, a member of new class of drugs, used to treat hypertension [2]. We report here the first case of lithium toxicity in a patient taking losartan.

A 77-year-old woman had been taking lithium carbonate 625 mg daily (and diazepam 10 mg) for a manic-depressive psychosis diagnosed in 1981. Her plasma lithium level had been stable for many years. It was 0.63 mmol/l in June 1996 (therapeutic range: 0.5–0.8 mmol/l). Breast carcinoma had been treated with tamoxifen (20 mg daily) for 15 years. Hypertension, found in 1988, had been treated with nifedipine (30 mg daily). In July 1996, persisting high blood pressure (180/100 mm Hg) led to addition of losartan (50 mg daily). Serum creatinine was 90 μmol/l (clearance of creatinine: 60 ml/min). Five weeks later, the patient was hospitalized with a 10-day history of ataxia, dysarthria, and confusion. Her plasma lithium concentration was 2 mmol/l. Serum creatinine was 108 μmol/l (clearance of creatinine: 53 ml/min). No other cause of lithium intoxication was found. Lithium and losartan were stopped. Symptoms had disappeared and her plasma lithium concentration had fallen to 0.55 mmol/l by 2 days after drug withdrawal. Lithium therapy was then restarted (375 mg daily), with nicardipine 100 mg daily. One week later, the plasma lithium level was 0.42 mmol/l and lithium carbonate was increased to 625 mg daily. One week later, the plasma lithium concentration was 0.77 mmol/l and serum creatinine 108 μmol/l. Lithium toxicity did not reappear.

In this patient plasma lithium levels rose when losartan was added to lithium therapy. The increase in lithium levels cannot be totally explained by the moderate renal insufficiency. More probably, increased renal lithium reabsorption, which occurs mainly at a proximal tubular site, is related to natriuresis associated with inhibition of aldosterone secretion induced by losartan. This inhibition is less complete with AT2-receptor antagonists than with ACE inhibitors. This could explain why the ACE inhibitor ramipril [3], but not losartan [4], decreases renal lithium excretion in the rat and why the fractional excretion of endogenous lithium was unchanged in healthy subjects taking losartan [5].

This case suggests a potential risk of lithium toxicity in elderly patients receiving both an AT2-receptor antagonist and lithium treatment.

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