

## Spirolactone and diabetic ketoacidosis

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### Summary

The authors describe a diabetic patient on spironolactone who, following a minor surgical procedure, developed ketoacidosis and life-threatening hyperkalaemia.

### Introduction

Spirolactone is a specific competitive antagonist of aldosterone, the most potent endogenous mineralocorticoid, which modifies renal electrolyte handling and is therefore commonly used as a diuretic in conditions associated with secondary hyperaldosteronism. In renal insufficiency, aldosterone antagonists may induce significant hyperkalaemia even if administered concurrently with a thiazide.

### Case history

A 57-year-old insulin-dependent diabetic man with alcoholic cirrhosis and ascites developed congestive cardiac failure. He was treated with bendrofluzide and spironolactone (100 mg daily consisting of two 25-mg tablets twice daily). He was admitted to hospital for cyclo-cryotherapy for diabetic

proliferative retinopathy. At this time he was in sinus rhythm and normotensive with no evidence of heart failure. Investigation showed ESR 80 mm in 1 hr (Westergren); plasma glucose (random) 10.3 mmol/l; blood urea 15.8 mmol/l; serum creatinine 270 mmol/l; 24-hr urinary protein 2.4 g; total serum protein 60 g/l; albumin 30 g/l; alkaline phosphatase 150 i.u./l (normal < 95). Plasma sodium 137 mmol/l; potassium 5.4 mmol/l; chloride 103 mmol/l; and bicarbonate 25 mmol/l. Chest X-ray examination showed left ventricular enlargement, ECG showed sinus rhythm and non-specific ischaemic changes. Insulin, digoxin and bendrofluazide were continued. Spirolactone 2 tablets twice/day was prescribed but he received 100-mg tablets instead of 25-mg tablets, i.e. a total of 400 mg daily for 3 days. On the day of the operation an 'early' breakfast was supplemented by 12 u. of soluble insulin and over the subsequent 12 hr he received dextrose (5%) i.v. At 1 p.m. he received atropine and papaveretum and was induced with thiopentone and tubocurarine. Anaesthesia was maintained on pethidine and lasted for 2 hr. Neostigmine and atropine were used as reversal relaxants. He was

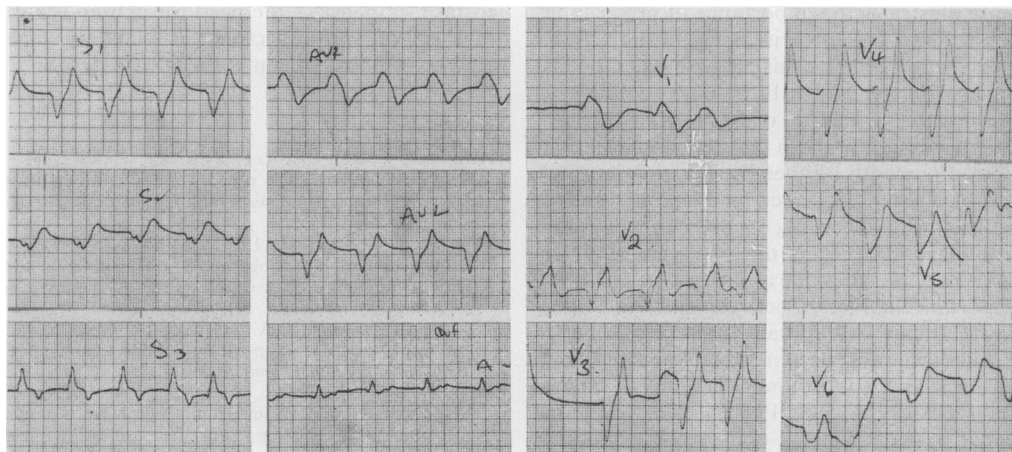


FIG. 1. Electrocardiograph (ECG) showing widening of QRS complexes and prominence of T waves.

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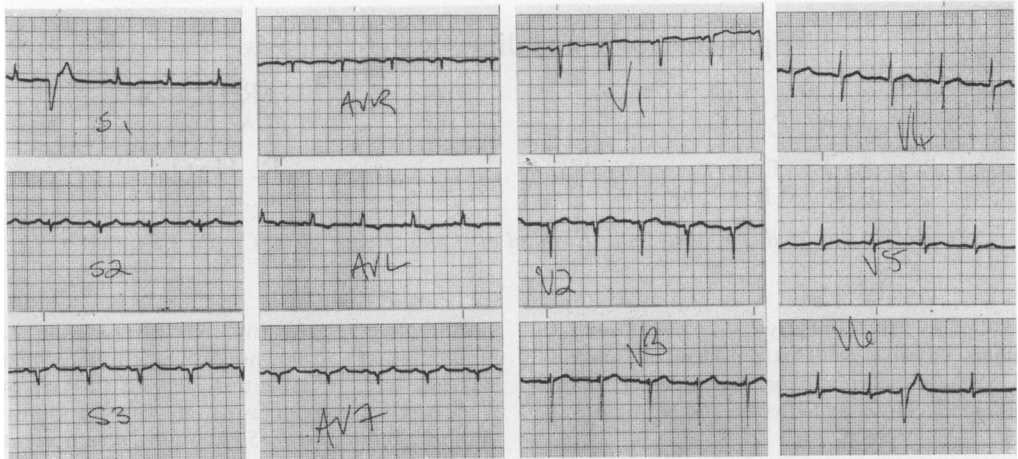


FIG. 2. Electrocardiograph (ECG) 24 hr later reverting to the pre-operative form.

given his normal evening dose of insulin (5 u. of Actrapid and 3 u. of Monotard) and a meal. He became drowsy and semicomatose. Plasma glucose was 43 mmol/l; sodium 118 mmol/l; potassium 8.3 mmol/l; urea 26 mmol/l; plasma osmolality 305 mmol; pH 7.13; bicarbonate 10.5 mmol/l; arterial oxygen pressure 10.8 kPa (83 mmHg) and arterial CO<sub>2</sub> pressure 4 kPa (31 mmHg) on room air; base deficit 18.9 mmol/l; ECG (Fig. 1) showed widening of QRS complexes and prominence of T waves. Spironolactone was withdrawn and he was resuscitated with fluids and insulin. ECG (Fig. 2) 24 hr later reverted to the pre-operative form, cardiac specific enzymes showing no evidence of myocardial infarction. He is now (2 years later) well.

### Discussion

This case illustrates the importance of prescribing the correct dose and the risk of spironolactone causing diabetic ketoacidosis. Spironolactone is available in 2 strengths which have equivalent bioavailability and a half-life of 20 hr (Karim *et al.*, 1976). There would have been marked accumulation of spironolactone with 4 times the patient's normal dose. It is suggested that there may be a need to prescribe this drug according to the patient's body weight. Similar difficulties of dose prescription have been reported with thyroxine and digoxin.

An important interaction between spironolactone and diabetes exists. Normal subjects during a glucose tolerance test become hypokalaemic, but diabetics increase their serum potassium (Gundersen, Bradley and Marble, 1954). This would be accentuated by worsening of control and has been emphasized for triamterene and amiloride (McNay and Oran, 1970), but not for spironolactone. Diabetics will also tend to have impaired renal

function which again will enhance the risk of potassium retention (Herman and Rado, 1966). Spironolactone may also cause acidosis owing to impairment of H<sup>+</sup> ion excretion and urinary acidification. Changes in potassium may be silent until of severe degree and the ECG may be misleading especially if hyponatraemia exists (Van Bucherne, 1957).

In this patient, despite the presence of adrenal antibodies, there was no evidence of adrenal hypofunction on a short tetracosactrin test, and the previously good diuretic response to spironolactone would be evidence against isolated aldosterone deficiency.

Close monitoring of diabetic control with an insulin infusion would have curtailed the medical emergency. The delicate state of potassium homeostasis emphasizes the need for extreme caution in the use of spironolactone in diabetics especially when worsening of control is anticipated.

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