

# Life-Threatening Hyperkalemia: A Complication of Spironolactone for Heart Failure in a Patient with Renal Insufficiency

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**S**pirolactone decreased the risk of death and hospitalization in patients with New York Heart Association class III or IV heart failure in the Randomized Aldactone Evaluation Study (RALES) (1). Based on the results of this trial, an increasing number of surgical patients with congestive heart failure can be expected to be taking spironolactone on admission for operation. The risk of hyperkalemia has raised concerns about the safety of spironolactone therapy for heart failure. In a recent report, 10% of patients treated with spironolactone in combination with angiotensin-converting enzyme (ACE) inhibitors for heart failure were hyperkalemic on admission to the emergency room (2). Physiologic conditions encountered during major operations may increase the risk for serious intraoperative hyperkalemia in surgical patients on spironolactone therapy.

## Case Report

A 74-yr-old, 100-kg man with an enlarging 6.4 cm infrarenal abdominal aortic aneurysm (AAA) was admitted for elective repair. The patient had hypertension, a previous myocardial infarction, congestive heart failure, and chronic renal insufficiency. Preoperative medications were metoprolol 25 mg *per os* (PO) bid, enalapril 10 mg PO bid, nifedipine 30 mg PO qd, furosemide 40 mg PO bid, spironolactone 25 mg PO bid, amiodarone 200 mg PO qd, atorvastatin 20 mg PO qd, aspirin 325 mg qd, and KCl 8 mmol PO bid. The serum sodium concentration was 141 mmol/L, potassium 5.5 mmol/L, chloride 103 mmol/L, bicarbonate 23 mmol/L, blood urea nitrogen 83 mg/dL, creatinine 2.6 mg/dL, glucose 65 mg/dL, and hemoglobin 12.9 g/dL 1 wk before the operation (Table 1). Dipyridamole technetium sestamibi myocardial perfusion tomographic imaging demonstrated a large fixed defect in the right and left circumflex coronary artery distribution. Echocardiography estimated the left ventricular ejection fraction to be

30%. The electrocardiogram showed sinus bradycardia and previous inferior myocardial infarction.

Before the operation, a right radial arterial catheter and an L3-4 epidural catheter were inserted. General anesthesia was induced by midazolam 5 mg IV, sodium thiopental 150 mg IV, fentanyl citrate 250  $\mu$ g IV, and cisatracurium 20 mg IV and maintained with inhaled oxygen and isoflurane. Analgesia was provided by an infusion of ropivacaine 0.3% and fentanyl 3  $\mu$ g/mL at 6 mL/h via the epidural catheter. A pulmonary artery catheter inserted after the induction of general anesthesia measured a pulmonary artery pressure of 52/36 mm Hg, central venous pressure of 11 mm Hg, and cardiac output of 2.79 L/min at an arterial blood pressure of 113/64 mm Hg and heart rate of 40 bpm.

Before the skin incision, an arterial blood sample demonstrated a potassium concentration of 7.0 mmol/L, ionized calcium of 1.22 mmol/L, glucose of 117 mg/dL, and a pH value of 7.36 (Table 1). Repeat testing of a second blood sample measured a potassium concentration of 6.8 mmol/L. Aortic cross-clamping was delayed, and the patient was treated for hyperkalemia with dextrose 12.5 g IV, insulin 20 IU IV, furosemide 100 mg IV, and dextrose 5% IV infusion at 60 mL/h. In addition, dopamine 2  $\mu$ g  $\cdot$  kg<sup>-1</sup>  $\cdot$  min<sup>-1</sup> IV was started. The plasma potassium concentration decreased to 5.2 mmol/L over the next hour and permitted the operation to continue (Table 1).

The aorta was cross-clamped below the renal arteries for a duration of 61 min. The infrarenal AAA was repaired with a 20-mm Dacron tube graft. The patient received normal saline 2600 mL IV and 225 mL of cell saver blood during the operation. The estimated blood loss was 800 mL, urine output was 1200 mL (480 mL/h), and cardiac output was 5.94 L/min at the end of the operation. The serum potassium concentration on arrival to the surgical intensive care unit was 4.9 mmol/L. The patient was discharged from the hospital on postoperative Day 4 on metoprolol, nifedipine, amiodarone, atorvastatin, furosemide, aspirin, and spironolactone 25 mg qd. The serum potassium concentration was 3.8 mmol/L, blood urea nitrogen concentration was 22 mg/dL, and creatinine was 1.4 mg/dL at the time of hospital discharge (Table 1).

## Discussion

The detection of serious intraoperative hyperkalemia in a patient being treated with spironolactone in combination with enalapril before aortic cross-clamping for repair of an AAA was fortunate. Lower extremity

Accepted for publication March 6, 2002.

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DOI: 10.1213/01.ANE.0000020694.65934.79

**Table 1.** Laboratory Values

	Preop Days -7	Intraop <sup>a</sup> Days				Postop Days			
		0	0	0	0	1	2	3	5
Time (AM)	-	8:50	9:20	9:55	10:40	-	-	-	-
Arterial Blood									
pH values	-	7.36	-	7.32	7.23	7.36	-	-	-
PCO <sub>2</sub> (mm Hg)	-	43	-	43	51	37	-	-	-
PO <sub>2</sub> (mm Hg)	-	387	-	367	251	271	-	-	-
Electrolytes									
Na <sup>+</sup> (mmol/L)	141	139	138	137	140	141	141	144	141
K <sup>+</sup> (mmol/L)	5.5	7.0	6.3	5.2	4.6	4.9	5.2	4.5	3.8
Cl <sup>-</sup> (mmol/L)	103	105	-	105	109	114	112	114	111
HCO <sub>3</sub> <sup>-</sup> (mmol/L)	23	25	-	22	23	19	19	21	23
Other									
BUN (mg/dL)	83	-	-	-	-	86	55	34	22
CRE (mg/dL)	2.6	-	-	-	-	2.3	1.8	1.5	1.4
GLU (mg/dL)	65	117	236	135	81	68	133	132	80
HGB (g/dL)	12.9	12.1	NA	10.5	9.7	10.2	10.1	8.7	8.9

<sup>a</sup> Aortic cross clamp was applied at 9:24 AM and removed at 10:25 AM.

BUN = blood urea nitrogen; CRE = creatinine; GLU = glucose; HGB = hemoglobin.

ischemia, metabolic acidosis, or renal impairment during temporary cross-clamping of the abdominal aorta may cause transient increases in the serum potassium concentration. If unrecognized, further increases in the serum potassium concentration on lower extremity reperfusion after removal of the aortic cross-clamp may have led to life-threatening conditions or even cardiac arrest. Preoperative detection of hyperkalemia permitted prompt treatment to normalize the serum potassium concentration before aortic cross-clamping.

Suspicion for hyperkalemia prompted the measure of serum potassium concentration immediately before operation. In a study of 25 patients treated with spironolactone and ACE inhibitors that defined serious hyperkalemia as a potassium concentration >6 mmol/L, the mean daily dose of spironolactone was 57 mg, the mean age of patients was 74 years, and the mean serum creatinine concentration was 3.8 mg/dL (2). The cause of renal insufficiency in this group of patients was dehydration in 12 patients and worsening of congestive heart failure in nine patients. In another case series, intravascular volume depletion and acute renal failure were frequent precipitating conditions for fatal or life-threatening hyperkalemia in patients with heart failure treated with spironolactone and ACE inhibitors (3). Renal insufficiency, advanced age, large doses of spironolactone, and concurrent administration of potassium supplements were also frequent features in other reported cases of hyperkalemia associated with spironolactone use (4-7). In retrospect, decompensated heart failure between the time of preoperative testing and admission for operation may have contributed to the increase in serum potassium concentration. Perioperative medical management improved the cardiac output

and decreased the serum creatinine concentration from a preoperative value of 2.6 mg/dL to 1.4 mg/dL at the time of hospital discharge.

Because aldosterone is important for regulating potassium homeostasis, the potential for hyperkalemia caused by spironolactone has generated concern, especially when used in the complex setting of heart failure (2-7). This concern was not evident in the RALES trial, which reported an incidence of serious hyperkalemia of only 2% in the spironolactone treatment group that was not different from the 1% incidence observed in the placebo group (1). However, in the RALES trial, the mean dose of spironolactone was only 26 mg/d, potassium concentrations were monitored frequently, potassium supplements were restricted, and patients with creatinine concentrations >2.5 mg/dL or serum potassium concentrations >5.0 mmol/L were excluded from treatment (1). In practice, the potential for hyperkalemia increases as the use of spironolactone for heart failure increases, treatment criteria are liberalized, larger doses of the drug are prescribed, and patients encounter conditions that predispose to hyperkalemia.

Identifying patients on spironolactone therapy at risk for hyperkalemia and laboratory testing immediately before the operation may increase the chances of detecting life-threatening hyperkalemia and increase the effectiveness of treatment. Risk factors for hyperkalemia as a consequence of spironolactone therapy for heart failure include renal insufficiency, dehydration, advanced age, a spironolactone dose larger than 25 mg/d, use of potassium supplements, and worsening heart failure. Despite a satisfactory outcome in the reported case, the safety of proceeding with the operation after the acute detection and treatment of serious

hyperkalemia in a patient with renal insufficiency receiving spironolactone requires further validation.

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