SHORT REPORT

Hypokalaemia and sudden cardiac death—lessons from implantable cardioverter defibrillators

Micha Maeder, Hans Rickli, Christian Sticherling, Regula Widmer, Peter Ammann

Emerg Med J 2007;24:206–208. doi: 10.1136/emj.2006.044073

The cases of four patients experiencing ventricular arrhythmia secondary to drug-induced hypokalaemia requiring treatment by a previously implanted cardioverter defibrillator (ICD) are reported here. In three cases, hypokalaemia developed within a short period of time after modification of diuretic regimen with loop and thiazide diuretics had been carried out or potassium-sparing drugs had been withdrawn. In one patient, hypokalaemia occurred after months of treatment with several potassium-sparing and non-potassium-sparing diuretics. The fact that the combination of thiazide and loop diuretics can be associated with pronounced hypokalaemia and life-threatening arrhythmias, which may be terminated by device treatment in patients with an ICD but may be fatal in patients with structural heart disease but without an ICD, is highlighted here. Prompt recognition and correction of hypokalaemia is mandatory if such patients present to the emergency department.

Non-potassium-sparing diuretics—that is, loop and thiazide diuretics—form a cornerstone in the treatment of patients with hypertension and congestive heart failure. Although this therapy is very efficacious with respect to blood pressure reduction and relief of oedema and pulmonary congestion, it can be associated with significant hypokalaemia,¹ which in turn increases cardiac excitability and thus the risk for ventricular arrhythmia.² We herein present a case series of four patients admitted within a period of only a few months owing to hypokalaemia-triggered life-threatening ventricular arrhythmia requiring intervention by a previously implanted cardioverter defibrillator (ICD).

CASE REPORTS

Case 1

A 55-year-old man with a history of arrhythmogenic right ventricular cardiomyopathy, severely impaired right ventricular function and recurrent peripheral oedema, coronary artery disease, and prophylactic ICD implantation 18 months previously was admitted because of several shocks. Urgent device interrogation revealed six sustained ventricular tachycardia terminated by appropriate ICD shocks (fig 1). Medical treatment consisted of acetylsalicylic acid 100 mg, amiodarone 200 mg, simvastatin 20 mg, torasemide 50 mg, spironolactone 25 mg, valsartan 160 mg, metolazone 5 mg and insulin. One month earlier, the torasemide dose had been increased from 10 to 50 mg, and metolazone treatment had been started. Laboratory analysis revealed a serum potassium concentration of 2.9 mmol/l, and serum creatinine had markedly increased (231 µmol/l as compared with 84 µmol/l 9 months ago). Metolazone was stopped, careful hydration was administered and potassium supplements were given for some days. Two weeks later, serum potassium was 4.1 mmol/l and serum creatinine was 151 µmol/l. In the following 6 months, no further shocks occurred.

Case 2

A 64-year-old man with a history of coronary artery bypass grafting underwent implantation of a biventricular ICD system for severely depressed left ventricular ejection fraction, left-bundle-branch block, and dyspnoea New York Heart Association class III despite optimised medical treatment. Device interrogation performed after two ICD shocks revealed two episodes of ventricular tachycardia with appropriate ICD treatments. Laboratory analysis showed significant hypokalaemia (serum potassium 2.6 mmol/l). Serum creatinine was within the range of previous studies (118 µmol/l). The serum potassium concentration had been normal (3.9 mmol/l) 1 week previously. Drugs administered to the patient included perindopril 2 mg, furosemide 125 mg, metolazone 5 mg, pravastatin 40 mg, acetylsalicylic acid 100 mg, phenprocoumon and spironolactone 25 mg. As the latter drug had induced painful gynaecomasty, there was no regular intake in the past weeks, however. Metolazone was stopped, furosemide was replaced by torasemide 20 mg and potassium supplements were given. In the following 3 months, no further shocks occurred.

Case 3

A 72-year-old woman with a history of successful open commissurotomy for rheumatic mitral stenosis, hypertensive heart disease with preserved left ventricular systolic function but diastolic heart failure and ICD implantation for recurrent sustained ventricular tachycardia in the absence of significant coronary artery disease was referred because of an electrical storm with three ICD shocks within a few minutes. Medical treatment consisted of phenprocoumon, atenolol 50 mg, furosemide 40 mg, and a combination of spironolactone 75 mg and butizide 7.5 mg. The latter drug combination had been started only a few days before the event. The patient was found to have a potassium level of 3.2 mmol/l, and thus the diuretic regimen was changed to torasemide 10 mg and spironolactone 50 mg. Three days later, serum potassium level was 4.3 mmol/l. During the next 3 months, no further ICD shocks occurred. Then, the patient was readmitted due to another three appropriate ICD shocks due to ventricular tachycardia. Laboratory analysis revealed a serum potassium level of 3.2 mmol/l. By accident, the patient had been given again a combination consisting of spironolactone 50 mg and butizide 5 mg instead of spironolactone 50 mg alone. No further shock occurred after butizide was stopped.

Case 4

A 78-year-old man with an ICD implanted 7 years ago due to coronary artery disease, moderately depressed left ventricular systolic function (left ventricular ejection fraction 40%) and recurrent ventricular tachycardia was referred for urgent control of the device. Interrogation revealed five sustained ventricular tachycardia, each terminated by ventricular over-

Abbreviation: ICD, implanted cardioverter defibrillator

Figure 1 Intracardiac ECG (upper channel) from a single chamber implantable cardioverter defibrillator (ICD) in patient 1 (serum potassium 2.9 mmol/l) showing ventricular tachycardia (VT, heart rate 158 beats/minute), terminated by a 34.8-J shock (*) delivered by the ICD. SR, sinus rhythm.

pacing (fig 2). The patient was taking atenolol 50 mg, pantoprazole 40 mg, acetylsalicylic acid 100 mg, isosorbide-mononitrate 60 mg, spironolactone 25 mg, amiloride 5 mg, hydrochlorothiazide 50 mg and furosemide 40 mg. Serum potassium was 2.6 mmol/l and serum creatinine did not differ significantly from previous values (106 μ mol/l). All non-potassium-sparing drugs were replaced by torasemide 10 mg, and potassium supplements were given for some days. Two weeks later, serum potassium had normalised (3.9 mmol/l). There were no further shocks in the following months.

DISCUSSION

Whereas earlier studies have shown a dose-dependent relationship between the use of non-potassium-sparing diuretics and risk of cardiac arrest and arrhythmic death,³ a recently published large-scale trial did not provide evidence for increased mortality in patients taking moderate doses of thiazide diuretics and caused new enthusiasm for this class of drugs.⁴ In fact, currently used thiazide doses are comparatively low and their long-term use for treatment of hypertension has been shown to be associated with only moderate potassium-lowering effects (0.2–0.5 mmol/l when using 12.5–25 mg hydrochlorothiazide).⁵ However, the situation in patients with congestive heart failure taking a combination of diuretics is different. Whereas loop diuretics block the sodium-potassium-chloride transporter at the proximal tubule, and thus impair sodium reabsorption with consecutively increased sodium

delivery to the collection tubules and increased potassium secretion, thiazide diuretics affect the more distally located electroneutral sodium-chloride transporter.⁶ In patients receiving long-term treatment with loop diuretics, hypertrophy of distal nephron segments with concomitant increased sodium reabsorption and decreased diuresis occurs (diuretic tolerance). Additional administration of a thiazide blocks sodium reabsorption at the nephron sites where the hypertrophy has occurred, and thus leads to a pronounced diuretic and kaliuretic response (sequential nephron blockade).⁶ Other factors promoting hypokalaemia may be withdrawal of inhibitors of the renin-angiotensin-aldosterone system (increased kaliuresis), withdrawal or dose reduction of β blockers or inhalation of β_2 -agonists, respectively (potassium shift from the extracellular into the intracellular space), new-onset insulin treatment (shift), or concomitant diseases such as diarrhoea (non-renal potassium loss).

Recent publications have alerted clinicians to avoid hyperkalaemia in patients with congestive heart failure taking several drugs blocking the renin-angiotensin-aldosterone system.^{7,8} However, the danger of hypokalaemia should not be neglected either. Unnecessary ICD shocks cause psychological harm in the affected patients and avoidable costs due to emergency visits and hospitalisations, as well as earlier end of life of the battery.

However, although we present a series of four patients with ICDs, they are not the real focus of our study. Our report

Figure 2 Intracardiac ECG (upper channel) from a single chamber implantable cardioverter defibrillator in patient 4 (serum potassium level 2.6 mmol/l) showing ventricular tachycardia (VT, heart rate 171 beats/minute), terminated by antitachycardia pacing (ATP). SR, sinus rhythm.

represents a form of pseudo-experimental study showing the deleterious effects of hypokalaemia in patients with structural heart disease very clearly. The relationship between thiazides, hypokalaemia and sudden cardiac death had been known for years.³⁻⁹ But the ICD technology allows now to prove what had been suspected for a long time from epidemiological studies. The combination of drugs reported herein and the dosages of diuretics appear to be uncommon, but these patients have been admitted within a period of only few months, and thus reflect the real life. There are many other patients with severe structural heart disease and similar drug regimens but without an ICD. These patients may present with life-threatening arrhythmia, and prompt recognition and correction of the underlying trigger is mandatory.

In conclusion, hypokalaemia is an important differential diagnosis in patients with structural heart disease presenting after repeated ICD shocks, and it is an even more serious condition in those without ICD, as it may promote fatal arrhythmia.

Authors' affiliations

Micha Maeder, Hans Rickli, Regula Widmer, Peter Ammann, Division of Cardiology, Department of Internal Medicine, Kantonsspital St Gallen, Switzerland

Christian Sticherling, Division of Cardiology, University Hospital Basel, Basel, Switzerland

Funding: None.

Competing interests: None.

Informed consent was obtained for publication of the patients' details in this report.

Correspondence to: Dr M Maeder, Division of Cardiology, University Hospital Basel, Petersgraben 4, CH-4031 Basel, Switzerland; micha.maeder@bluewin.ch

Accepted 16 November 2006

REFERENCES

- 1 Gennari FJ. Hypokalemia. *N Engl J Med* 1998;**339**:451–8.
- 2 Macdonald JE, Struthers AD. What is the optimal serum potassium level in cardiovascular patients? *J Am Coll Cardiol* 2004;**43**:155–61.
- 3 Cooper HA, Dries DL, Davies CE, et al. Diuretics and risk of arrhythmic death in patients with left ventricular dysfunction. *Circulation* 1999;**100**:1311–15.
- 4 ALLHAT Officers and Coordinators for the ALLHAT Collaborative Research Group. Major outcomes in high-risk hypertensive patients randomized to angiotensin-converting enzyme inhibitor or calcium channel blocker vs. diuretic: the Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT). *JAMA* 2002;**288**:2981–97.
- 5 SHEP Cooperative Research Group. Prevention of stroke by antihypertensive drug treatment in older persons with isolated systolic hypertension. *JAMA* 1991;**265**:3255–64.
- 6 Brater DC. Diuretic therapy. *N Engl J Med* 1998;**339**:387–95.
- 7 Svensson M, Gustafsson F, Galatius S, et al. Hyperkalaemia and impaired renal function in patients taking spironolactone for congestive heart failure: retrospective study. *BMJ* 2003;**327**:1141–2.
- 8 Juurlink DN, Mamdani MM, Lee DS, et al. Rates of hyperkalemia after publication of the randomized aldactone evaluation study. *N Engl J Med* 2004;**351**:543–51.
- 9 Siscovick DS, Raghunathan TE, Psaty BM, et al. Diuretic therapy for hypertension and the risk of primary cardiac arrest. *N Engl J Med* 1994;**330**:1852–7.