

Clinical Reports

Transient atrial fibrillation in hypertensive patients with thiazide induced hypokalaemia

M.K. Emara and A.M. Saadet

Department of Medicine, Mubarak Hospital, Kuwait.

Summary: During the previous 34 months, 3 hypertensive patients on long-term thiazide therapy were admitted to the medical department, Mubarak Hospital, Kuwait, with atrial fibrillation (AF) and hypokalaemia. They received potassium chloride by intravenous infusion, followed by oral therapy with reversion to sinus rhythm. There were no clinical, electrocardiographic, radiological, or echocardiographic signs of cardiac or pericardial disease, and the other usual cases of AF were also excluded. The contribution of thiazide-induced hypokalaemia to the occurrence of AF in our patients is discussed.

Introduction

Most thiazide-induced hypokalaemia is mild and its significance in otherwise healthy hypertensives is unclear. A serum potassium between 2.5–3.4 mmol/l was sustained over a 2-year period in 23% of patients (VAC study, 1972). Increasing evidence, however, points to the risk of developing cardiac arrhythmias in some of these patients (MRC trial, 1983). An increased incidence of ventricular fibrillation was also reported in hypokalaemic patients after acute myocardial infarction (Nordrehaug & Von der Lippe, 1983).

We report here 3 hypertensive patients on long-term thiazide therapy presenting with atrial fibrillation and hypokalaemia.

Patients

Clinical details are given in Table I. The three patients were on long-term chlorthalidone therapy, without potassium supplementation. A previous history of recurrent palpitations was obtained from the second patient only.

On admission, no signs of heart failure were present in any of the three patients, and the ventricular rate ranged between 120–140/minute.

When the results of serum electrolytes were available, potassium chloride, in a dose of 20 mmol 4 hourly

was given by intravenous infusion for the first 24 hours. This was replaced by 20 mmol oral slow release potassium chloride 6 hourly with monitoring of serum electrolytes. AF reverted to sinus rhythm, 5–10 hours after starting intravenous potassium therapy. When serum potassium reached 4 mmol/l, oral potassium was replaced by a potassium sparing diuretic. The dose of methyldopa was increased in patients (1) and (2), to obtain better control of blood pressure.

None of the three patients had any clinical, electrocardiographic, radiological or echocardiographic evidence of cardiac or pericardial disease. Thyroid function studies done in each case (including thyrotrophin releasing hormone stimulation test) yielded normal results.

Pulmonary embolism was excluded by the presence of normal arterial blood gases, and pulmonary perfusion scans. There were no clinical, electrocardiographic or laboratory signs suggestive of acute myocardial infarction in any of the cases. Other laboratory tests, including complete blood count, urine analysis, and biochemistry were normal apart from hypokalaemia and slight rise in bicarbonate. It was not possible to do a serum magnesium estimation.

During the follow-up period (11–34 months) serum electrolytes were within the normal range, and there was no history of palpitations suggestive of recurrence of atrial fibrillation.

Three months after discharge, a 24 hour Holter monitor was done for each patient. No significant abnormalities were detected in any of the records apart from occasional supraventricular and ventricular ectopic beats.

Correspondence: M.K. Emara M.B., D.M., D.C.V.D., F.R.C.P. (Ed), F.R.C.P. Dept. of Medicine, Faculty of Medicine, Kuwait University, P.O. Box 24923, Safat – 13110, Kuwait.

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Table I Clinical characteristics of the three patients

	<i>Case I</i>	<i>Case II</i>	<i>Case III</i>
Sex	Female	Male	Male
Age (years)	52	48	44
Antihypertensive therapy (daily)	Methyldopa 0.25g × 3 Chlorthalidone 50 mg	Chlorthalidone 100 mg	Methyldopa 0.25g × 2 Chlorthalidone 50 mg
Approximate duration of therapy (years)	3	3	8
Clinical presentation	Dizziness + Palpitations	Palpitations	Palpitations
Blood pressure on admission (mmHg)	160/110	170/100	170/115
Serum potassium on admission (mmol/l)	2.7	2.8	2.8
Serum bicarbonate (mmol/l)	28	28	27
Duration of AF after starting i.v. potassium (hours)	8	5	10
Duration of follow-up (months)	34	14	11

Discussion

Atrial fibrillation which may initially be paroxysmal, before becoming persistent, is a recognized complication of hypertension. In a group of hospitalized patients, hypertensive heart disease was present in 35% of cases with paroxysmal atrial fibrillation (Takahashi *et al.*, 1981). Atrial fibrillation occurs mainly in the presence of hypertensive heart disease and cardiac failure is usually present (Freidberg, 1966). The Framingham study revealed that hypertension unaccompanied by signs of left ventricular enlargement or cardiac failure is very weakly correlated with atrial fibrillation (Kannel *et al.*, 1982). There was no evidence of cardiac enlargement or cardiac failure in any of our patients. The relationship of atrial fibrillation to hypokalaemia is evidenced by the absence of any further clinically recognized episodes of atrial fibrillation during the follow-up period when serum potassium was maintained within the normal range. Most probably our patients had transient rather than paroxysmal atrial fibrillation and this makes 'lone' atrial fibrillation unlikely. Other causes of transient atrial fibrillation are pulmonary embolism, acute myocardial infarction, pericarditis, post-operative, and pneumonia (Sloan, 1982). There was no evidence of any of these in our patients.

Hypokalaemia is known to facilitate ectopic atrial and ventricular beats by either re-entry or automatic mechanisms (Schwartz, 1978). In the presence of ischaemic heart disease, mild hypokalaemia may lead to ventricular electrical instability and serious ventricular arrhythmias (Stewart *et al.*, 1985). In the

presence of an appropriate anatomical substrate in some patients, e.g. intra-atrial conduction defects or bypass, atrial fibrillation may also be induced (Moss, 1984). Its occurrence is favoured by accelerated repolarization of the atrial muscle, and such an electrophysiological change may result from hypokalaemia (Olsson, 1971).

Measuring whole body potassium in hypertensive patients receiving prolonged thiazide therapy revealed that a fall of 1.0 mmol/l in plasma potassium is usually associated with a reduction of about 20% of the total body potassium (Edmonds & Jasani, 1972). Our 3 patients were receiving a dose of chlorthalidone (a long acting diuretic), 4 times the ceiling antihypertensive dose (Silas, 1985). This might have contributed to the severity of potassium depletion.

The relationship between atrial muscle potassium and post-operative atrial fibrillation in cardiac patients was studied by taking pre-operative atrial biopsies (Ebert, 1970). Patients developing post-operative atrial fibrillation had significantly lower potassium than patients remaining in sinus rhythm.

Hypokalaemia is also considered one of the main causes of atrial fibrillation in paediatric age groups (Bellet, 1971).

Atrial fibrillation and atrial flutter are intimately related in terms of the fundamental mechanism involved in the genesis (Chung, 1983). It was possible in a hypertensive patient with atrial flutter, thiazide-induced hypokalaemia, and a clinically normal heart, to re-induce the arrhythmia after its termination, by

rapid atrial stimulation. This occurred only in the presence of hypokalaemia but not after its correction (Varriale *et al.*, 1983). The occurrence of atrial fibrillation in hypertensive patients without clinical evidence of hypertensive heart disease may be due to other cardiac or extracardiac causes. We believe that in our cases, thiazide-induced hypokalaemia acted as a main

factor in inducing atrial fibrillation, and suggests that this needs further study.

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