Successful haemodialysis in sotalol-induced torsade de pointes in a patient with progressive renal failure

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Introduction

Progressive renal failure can result in toxic plasma concentrations of drugs with primarily renal clearance. Sotalol, a β-blocking agent with class III (lengthening refractory period and QT time) antiarrhythmic properties, is largely excreted unchanged in the urine. It is indicated for supraventricular and ventricular tachycardia and prescribed with increasing frequency. QT prolongation is associated with torsade de pointes, a potentially lethal form of polymorphic ventricular tachycardia. We describe a patient with chronic sotalol therapy and progressive renal failure who developed torsade de pointes, successfully treated with haemodialysis and temporary transvenous electrical pacing.

Case report

A 47-year-old Asian man presented with hypoglycaemia. For the past 17 years he had been known to have hypertension and non-insulin-dependent diabetes mellitus, which were complicated by retinopathy and slow deterioration of renal function. Two years before admission he had an episode of left-sided heart failure due to paroxysmal atrial flutter, treated with electrical cardioversion, propafenone, and later sotalol. His medication on presentation included enalapril 20 mg, sotalol 80 mg t.i.d., digoxin 0.125 mg, insulin, bumetanide 3 mg b.i.d., and allopurinol. Laboratory results were as follows: glucose 1.4 mmol/l, Hb 8.5 g/dl, potassium 5.2 mmol/l, creatinine 870 μmol/l, BUN 24.1 mmol/l, albumin 21 g/l.

The endogenous creatinine clearance according to Cockroft and Gault [1] was 9.4 ml/min. An electrocardiogram (ECG) showed sinus rhythm 64 b.p.m. with prolonged QT, time of 0.6 s (QT time corrected for heart rate following Bazett’s formula, normally <0.4 s in males). After glucose was given intravenously the patient recovered but was admitted because of his deteriorating renal function with nephrotic syndrome, requiring preparation for renal replacement therapy. Sotalol and digoxin were continued.

During hospitalization episodes of syncope lasting 10–20 s were observed, not due to hypoglycaemia. A transthoracic echocardiogram, made to exclude cardiac emboli, showed short bouts of ventricular tachycardia without substantial cardiac output. During these periods the patient had syncope again. An ECG was made and is shown in Figure 1. K+ was 3.9, Ca2+ 2.09 mmol/l and Mg2+ 0.87 mmol/l. Sotalol-induced torsade de pointes starting in periods of slow sinus rhythm (55 beats per minute) in a patient with end-stage renal failure was diagnosed. Two periods of ventricular fibrillation required defibrillation. Sotalol and digoxin were discontinued. The digoxin concentration later proved to be under the therapeutic range (0.5 mmol/l).

We inserted a temporary ventricular pacemaker set at a minimum rate of 90 beats per minute to decrease the risk of bradycardia-induced recurrence of torsade de pointes. After haemodynamic stabilization haemodialysis was started to achieve enhanced sotalol elimination. Because of his long-standing uraemic situation dialysis was limited to 3 h to prevent the occurrence of convulsions; blood flow 200 ml/min; dialysate bicarbonate Gambro N-252-S (K+ 3.0 mmol/l with glucose), flow 500 ml/min, conductivity 14.0 cm/s2, ultrafiltration 100 ml/h for 3 h using Gambro F6 artificial kidney. A second haemodialysis treatment followed 16 h later. Heart rate and QT-time were monitored constantly and blood samples were frequently drawn.

After start of haemodialysis QTc time shortened in concert with sotalol concentrations. The patient still had sporadic non-sustained ventricular tachycardia for 5 days, but no further episodes of torsade de pointes were observed. A few days later a peritoneal dialysis catheter was inserted.

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Fig. 1. ECG showing slow sinus rhythm with prolonged QTc interval of 0.66 s, atrial tachycardia with a frequency of 180/min, and polymorphous ventricular tachycardia.

Fig. 2. Plasma sotalol concentrations (●) and QTc time (●) versus time. During haemodialysis (HD) both sotalol concentration and QTc time decreased quickly compared to non-dialysing periods.
Sotalol concentrations were determined using an high-performance liquid chromatography assay. Plasma sotalol concentrations are shown in Figure 2. Haemodialysis effectively reduced sotalol concentrations. The half-life of sotalol during haemodialysis was 4.5 h, thereafter the half-life without haemodialysis was 96 h.

Discussion

Sotalol is a racemic mixture of (+)-sotalol and (−)-sotalol, the (−)-sotalol has class II (β-blocking) activity. Both enantiomers have class III antiarrhythmic properties with inherent risk for torsade de points.

The incidence of torsade de pointes increases with increasing sotalol dose [2]. Therapeutic plasma concentrations range from 1 to 3.5 μg/ml [3]. Sotalol is moderately (0–40%) bound to plasma proteins [3,4]. Its elimination is largely by glomerular filtration with 75% of a dose being excreted unchanged in human urine. The $t_{1/2}$ of sotalol in patients with normal renal function varies from 7 to 18 h [3]. Sotalol plasma clearance strongly correlates with creatinine clearance ($r = 0.88$) [5]. In renal insufficiency half-life is markedly increased. Values ranging from 40 [6] to 100 h [7] have been reported.

Contrary to most other β-blocking agents sotalol is hydrophilic. It can be removed by haemodialysis during which $t_{1/2}$ was found to be 7 h [6]. We calculated half-life to be 4.5 h during the first period of dialysis in our patient. Haemodialysis has been shown to be successful in sotalol-induced torsade de pointes in a patient with acute sotalol-induced torsade de pointes during electro-physiological testing [8]. The renal function of this patient was not mentioned. Our patient had chronic sotalol therapy. When he developed torsade de pointes induced by a high plasma concentration of sotalol in end-stage renal failure, haemodialysis was successfully used for removing sotalol and preventing recurrence of torsade de pointes. After 37 h the $T_{c}$ time had normalized to 0.5 s, the maximal recommended $T_{c}$ time during sotalol therapy [9]. At that time the plasma sotalol concentration was 3.3 μg/ml. Without haemodialysis it was calculated to be 110 h before the plasma sotalol concentration would have declined to this level. Thus, haemodialysis shortened the period at risk of torsade de pointes by 73 h.

Considering the increasing use of sotalol, it is important to emphasize that in a patient with increasing renal failure sotalol dose should be adjusted to creatinine clearance. $T_{c}$ times should be monitored closely, and that haemodialysis can be used to shorten the period at risk of sotalol-induced life threatening episodes of torsade de pointes.

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References


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