

Drug-induced long-QT syndrome: a case report

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An elderly psychiatric female patient with a long-lasting severe resistant depression was referred for medical examination because of gastrointestinal complaints. The ECG revealed a strongly extended QT interval. No other cardiological abnormalities were observed. The patient's symptoms as well as the QT interval and biochemical abnormalities could be reduced by changing psychiatric drug treatment and reduction of concomitant medication. (*Neth Heart J* 2005;13:98-100.)

Key words: antipsychotic drugs, interactions, periodic control, long-QT syndrome

With interest we read the special article on drug-induced long-QT syndrome.¹ Attention is repeatedly being drawn to heart rhythm disturbances during administration of cardiac and noncardiac drugs²⁻⁴ including antipsychotics.⁵ Also in our own experience side effects of medication appear to be increasingly important, requiring regular consultation between psychiatrists, specialists in internal medicine and in clinical biochemistry and registrars in psychiatry.⁶ During the last decades we have developed guidelines for treatment with antipsychotic drugs and metabolic control of treated patients (table 1). Alongside biochemical monitoring, we also advise ECG control of patients treated with antipsychotic or antidepressive drugs including lithium. An upper limit for QTc of 500 ms is accepted and co-medication is carefully observed. We observe abnormalities in about 70% of 300 ECG controls per year. Because of induction of long QT intervals the use of a number of drugs, such

as thiorodazine and pimozide, has been abandoned in our clinic. However, psychiatric disorders are a severe burden for most patients and their families and treatment with antipsychotic or antidepressive drugs is often necessary. Risks associated with administration can be avoided to a great extent by repeated instruction of treating physicians and the use of guidelines (table 1) for somatic control of patients taking lithium, tegretol, leponex, tricyclic antidepressive drugs etc. Kidney and liver functions are periodically monitored. Careful attention is paid to the blood potassium level which easily tends to drop below 3.5 mmol/l due to the use of diuretics or laxatives, especially in female patients. No effects of grape fruit juice have been observed but the daily intake of litres of coffee and excessive smoking was supposed to influence the CYP3A4 enzyme system, as well as extreme physical exercise of agitated patients. The presence of congenital long QT interval or cardiac pathology was considered to be a contraindication for the administration of modern antipsychotic drugs.⁷ In such cases we advise the use of antipsychotics with strong D2-receptor affinity such as the phenothiazine derivative zuclopentixol, the butyrofenon derivative haloperidol and the atypical antipsychotic drug risperidone. Most experience with these drugs exists in the treatment of delirium. Alertness to side effects is always necessary.⁸

Our guidelines are frequently updated, based on, for instance, literature, practical experience and registration of complications. Despite the efficacy of this policy and all precautions, the choice of optimal therapy can still be difficult as is illustrated by the following case report.

Case report

A female patient aged 59 years had been treated for many years on account of a bipolar disturbance which, in recent years, had developed into a serious therapy-resistant depression. She was referred by her treating psychiatrist for medical consultation because of persistent diarrhoea and recent significant weight gain. On first examination no organic cause could be found. Low blood glucose and potassium levels were observed once; later values were normal. Initially she was treated

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Table 1. Guidelines for monitoring and control of patients treated with psychopharmaceutics (control intervals in months).*

	Blood level	Leucocytes	Liver enzymes**	Blood creatinine	Blood Na, K	Glucose	Other	ECG	Body weight
Lithium	3 m	-	-	6 m	6 m	6 m	Ca, TSH	6 m	6 m
Carbamazepine / Oxcarbazepine	6 m	6 m	6 m	6 m	6 m	6 m	-	6 m	6 m
Valproate	6 m	6 m	6 m	-	-	6 m	-	6 m	6 m
Clozapine	6 m	1 m	6 m	6 m	6 m	6 m	-	6 m	6 m
Tricyclic antidepressants	6 m	6 m	6 m	6 m	6 m	-	-	6 m	6 m

* Based on experience and relevant literature, including the Dutch Society of Psychiatry's 1998 Guidelines for the use of lithium, carbamazepine and valproic acid and the 2001 Guideline for bipolar disorders, and Nolen's Pharmacotherapy in manic-depressive disorders.¹⁰

** ASAT, ALAT, γ GT and alkaline phosphatase.

Na=sodium, K=potassium, Ca=calcium, TSH=thyroid-stimulating hormone, m=month, ASAT=aspartate aminotransferase, ALAT=alanine transaminase, GT=glutamyl transpeptidase.

with mirtazapine which was later replaced by venlafaxine because of insufficient effect. As the patient felt unwell and complained of pectoral angina and pallor, medical consultation was requested again. The ECG taken at that point showed a long QT interval of 628 ms; QTc 607 ms (figure 1). Consultation with the cardiologist revealed no other cardiac abnormalities. No indications for congenital LQTS could be detected. The patient's father died from a malignancy (age 78) and her mother died from

metastasis of breast carcinoma (age 72). The patient did not smoke or drink alcohol and had given birth to two healthy children. Venlafaxine therapy was now replaced by lithium: 800 mg taken in the evening. A third reference consultation revealed lithium intoxication (3.5 mmol/l, reference values 0.8-1.3 mmol/l). On persistent anamnesis the patient admitted taking extra medication: 2400 mg ibuprofen daily because of pain due to arthrosis deformans, and 'a number of vitalising capsules' taken to lose weight. The latter most

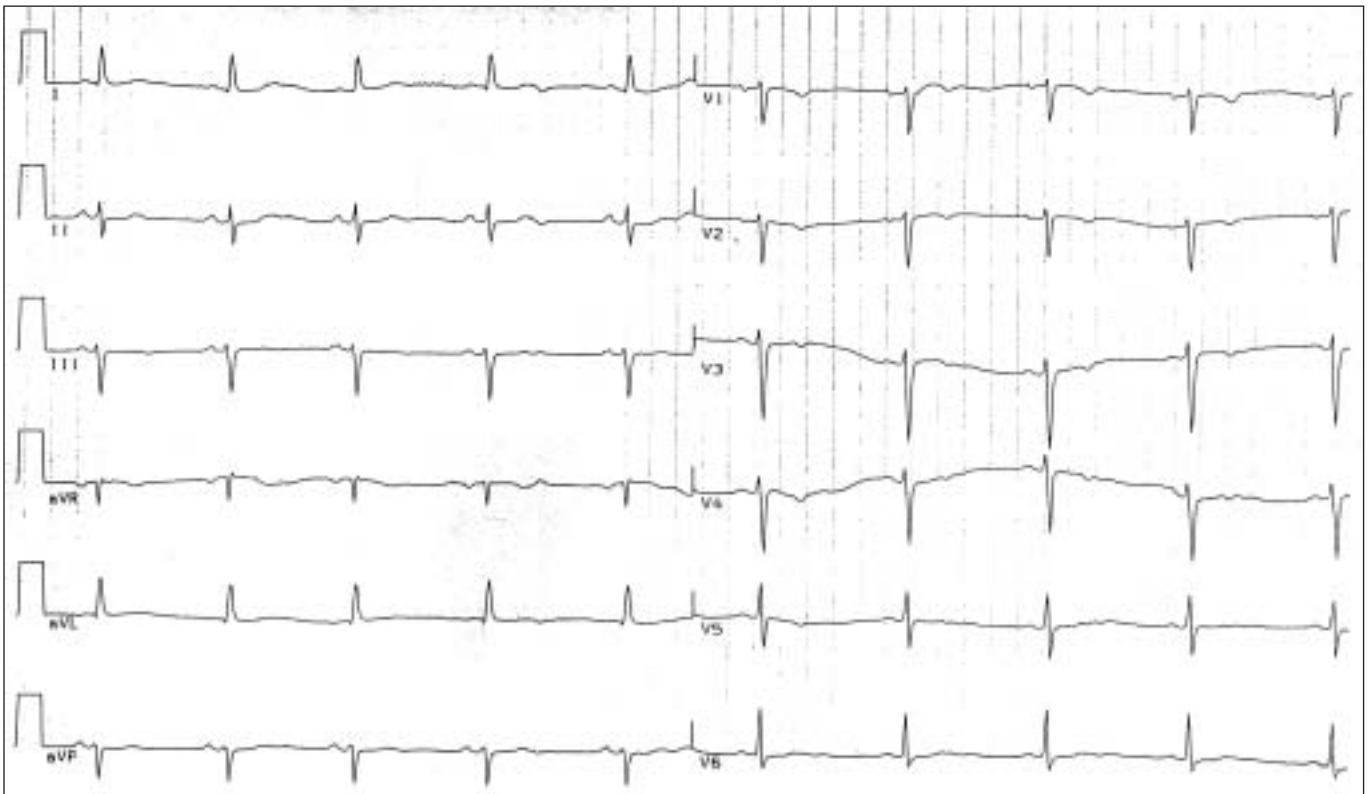


Figure 1. Patient's ECG patterns during drug-induced long-QT syndrome. QT/QTc 628/607 ms.



Figure 2. Patient's ECG patterns after discontinuing LQTS inducing drug treatment. QT/QTc 340/420 ms.

probably contained orlistat, an inhibitor of the enzyme lipase, thus preventing the hydrolysis and subsequent uptake of triglycerides from the intestine. This could explain her diarrhoea and potassium loss causing low blood potassium values. Moreover, interaction with venlafaxine could not be excluded. On substituting lithium therapy with valproic acid and omitting the 'vitalising capsules', the patient's general condition improved and the QT/QTc interval was reduced to 360/420 ms (figure 2). Her complaints of pain from arthrosis deformans could be relieved by careful administration of NSAIDs.

Conclusion

It can be concluded that the evaluation of side effects and interactions of drugs requires much effort and experience. Moreover, the generally increasing age of the population complicates both psychiatric and somatic therapies and its interactions. Especially the last decade can be characterised by rapid developments in psychotherapeutic possibilities and growth of psychopharmacology.⁹ New drugs have become available and other drugs have been withdrawn, despite sometimes positive experiences, because of side effects as observed in our patient. For example, we successfully treated 42 patients with sertindol without complications, but the

drug is no longer available. Choosing drugs for optimal treatment is certainly not an easy task. Careful observation of patients including periodic control of somatic functions is generally advised and in our control proved to be successful. ■

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