

Prolonged QT interval after fexofenadine overdose in the presence of hypokalemia and hypocalcaemia

在低血鉀及低血鈣下，過量的非索那定延長 QT 間期

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A 23-year-old healthy woman was admitted to our emergency department because of syncope and unconsciousness. She had taken 20 tablets of fexofenadine (total 2400 mg) and 9 tablets of furosemide (total 360 mg) for suicide. The electrocardiogram demonstrated bradycardia (48/min) and markedly prolonged QT_c interval (684 msec). Endotracheal intubation and nasogastric tube insertion were performed. Gastric lavage was implemented and activated charcoal was given. A transient pacemaker was implanted. Hypokalemia and hypocalcaemia were also present and the electrolyte disturbances were corrected. The heart rate and QT_c interval returned to normal limits after treatment. She stayed in our hospital for seven days. She recovered completely and ventricular arrhythmia was not seen during the hospitalization period. (*Hong Kong j.emerg. med.* 2010;17:75-78)

一名 23 歲健康女子因暈厥及昏迷而被送進急症室。她自殺服下 20 粒非索那定（共 2400 毫克）及 9 粒呋塞米（共 360 毫克）。心電圖展示心搏徐緩（每分鐘 48 次）及 QT_c 間期顯著地延長（684 毫秒）。進行了氣管內插喉、插入鼻胃管、洗胃、給與活性炭及植入暫時性的起搏器；並糾正了電解質的紊亂：低血鉀及低血鈣。治療後心率及 QT_c 間期回復正常範圍內。她在醫院住了 7 天。她完全康復，在住院期間，沒有心室心律失常。

Keywords: Electrolytes, furosemide, histamine H₁ antagonists, hyponatremia, syncope

關鍵詞：電解質、呋塞米、H₁ 抗組織胺、低血鈉、暈厥

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Introduction

Some first- and second-generation H₁-receptor antagonists are associated with prolongation of corrected QT (QT_c) interval, and in rare cases ventricular arrhythmias. It has been reported that terfenadine used concomitantly with hepatic metabolism inhibitors is associated with lethal torsades de pointes and ventricular tachycardia.¹ Fexofenadine, a carboxylate metabolite of terfenadine, is known to have no significant effect on QT or QT_c interval and to have no cardiovascular adverse effect.¹⁻³ We present a case who had syncope related to bradycardia with

markedly increased QT_c interval after the intake of a high dose of fexofenadine. In addition, the patient had also taken 360 mg furosemide and hypokalemia and hypocalcaemia were also present when she was admitted to the hospital.

Case report

A 23-year-old woman was admitted to our emergency department with syncope and unconsciousness in February 2008. She did not have any past systemic disease. Her relatives said that she had taken 20 tablets (120 mg each, total 2400 mg) of fexofenadine (Fexofen, Sanovel, Istanbul, Turkey) and 9 tablets (40 mg each, total 360 mg) of furosemide (Desal, Umut Ilaç, Istanbul, Turkey) for suicide, ten hours before admitting to our hospital. Cardiac resuscitation (3 mg atropine and 3 mg epinephrine used concomitantly) and gastric lavage were performed, four hours after taking these drugs, at an outer state hospital. The Glasgow Coma Scale was 3, the pupillary

light reflex was negative bilaterally, and the pupils were fixed and dilated. Endotracheal intubation was immediately performed with concomitant positive pressure ventilation initiated. Her initial blood pressure was 50/30 mmHg, and the heart rate was 40 beat/min. The first electrocardiogram demonstrated bradycardia (48/min) and markedly prolonged QT_c interval (Figure 1). The QT_c interval was calculated manually with Bazett's formula by using lead II and was timed to be 684 msec. A nasogastric feeding tube was inserted, gastric lavage was implemented and activated charcoal was given immediately. Then, the patient was transferred to the intensive care unit. A transvenous temporary pace-maker was implanted via the femoral vein and it stayed for 12 hours. The pace-maker was set to demand mode at 60 beat/min. When the patient was admitted to the hospital, a biochemical evaluation was done and hyponatremia, hypokalemia and hypocalcaemia were detected. Her laboratory data were as follows: sodium 123 mEq/L, potassium 3.3 mEq/L, calcium 6.4 mg/dL, blood urea nitrogen 15 mg/dL, creatinine 0.86 mg/dL, and haemoglobin

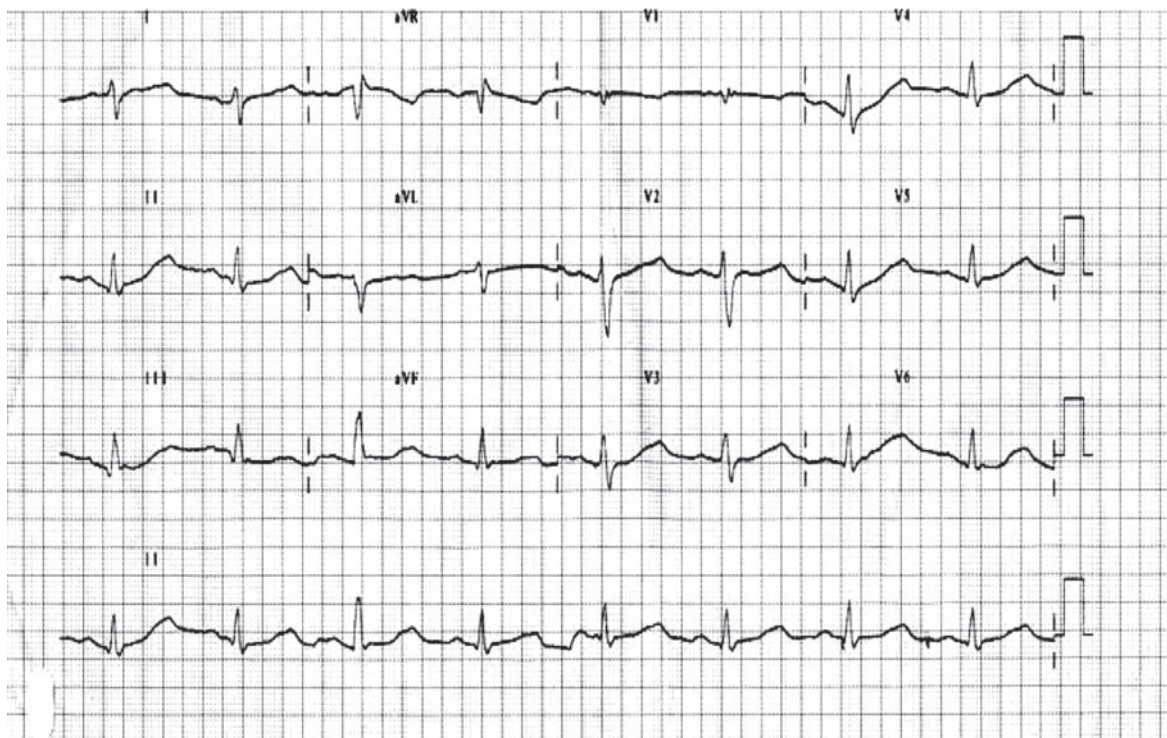


Figure 1. ECG showing bradycardia and markedly prolonged corrected QT interval.

12 g/dL. Transthoracic echocardiography was done and did not reveal any abnormal finding. 100 mEq potassium chloride, 4 g calcium chloride and 3500 ml 0.9% saline were administered intravenously in 24 hours.

In the follow-up period, 19 hours after the admission, the patient regained consciousness and was extubated. Her blood pressure was 120/80 mmHg and heart rate was 92/min. After replacements, the serum sodium, potassium and calcium levels returned to normal limits (sodium 138 mEq/L, potassium 4.2 mEq/L, calcium 8.5 mg/dL). The QT_c interval normalised approximately 12 hours after the commencement of electrolyte replacement (i.e. 4-6 hours after the electrolyte levels returned to normal). The transient pace-maker was then removed. She stayed for seven days in our hospital and ventricular arrhythmia was not detected during the hospitalisation period. She recovered completely and was discharged.

Discussion

The causes of prolonged QT_c are: congenital (long QT syndrome) or acquired cardiac diseases (ischaemic heart disease, cardiomyopathy, hypertension, myocarditis, valvular diseases), cerebrovascular diseases (haemorrhage, stroke), systemic diseases (renal, liver), electrolyte abnormalities (hypokalemia, hypomagnesaemia, hypocalcaemia), and the effect of drugs. Drugs that most frequently cause prolonged QT_c and torsades de pointes are: antiarrhythmic drugs (quinidine, procainamide, disopyramide, mexiletine, encainide, flecainide, amiodarone, bretylium, sotalol), psychiatric drugs (thioridazine, chlorpromazine, haloperidol, lithium, tricyclic antidepressants; amitriptyline, imipramine, doxepin), antihistamines (terfenadine, astemizole, ebastine), antimicrobial and antimalarial drugs (erythromycin, clarithromycin, ketoconazole, quinine, chloroquine, amantadine).^{2,3} The individual risk and potential of a pharmacologic substance to prolong the QT interval are not predictable.^{2,3} (Please visit www.qtdrugs.org, www.longqt.org and www.torsades.org websites for QT-prolonging drug lists and list of drugs to be avoided by patients with long QT syndrome).

Second-generation, non-sedating antihistamines are commonly used for allergic conditions. Terfenadine and astemizole have been associated with prolongation of the QT interval and development of ventricular arrhythmias, such as torsades de pointes.⁴ Several studies showed that blockade of potassium channels, particularly IKr, by antihistamine drugs leads to prolongation of the QT interval. However, there is no linear relationship between the degree of QT interval prolongation and the likelihood of development of torsades de pointes.⁵

Fexofenadine, a carboxylate metabolite of terfenadine, has been used for the treatment of seasonal allergic rhinitis and chronic idiopathic urticaria for more than 10 years. Controlled trials have demonstrated that fexofenadine does not prolong QT_c and does not cause torsades de pointes or any ventricular arrhythmia.⁶⁻⁸ Up to date, there is only one case report which revealed increased QT_c interval and ventricular tachycardia associated with fexofenadine.⁹

Conclusion

We report a young and healthy woman who suffered from bradycardia and markedly increased QT_c interval related to the intake of a very high dose of fexofenadine (2400 mg in total) in the presence of hypokalemia and hypocalcaemia. She had also taken furosemide (360 mg in total) and the electrolyte disturbances were due to the furosemide overdose. After correction of the electrolyte imbalance, the heart rate and QT_c interval returned to normal limits. Our patient's bradycardia and markedly increased QT_c interval may not only be due to the hypokalemia and hypocalcaemia but also the coexistence of fexofenadine. It is possible that the fexofenadine overdose might have contributed to such findings in the present case.

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