

Arrhythmogenic effect of flecainide toxicity

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Abstract

Flecainide is a class 1C antiarrhythmic drug especially used for the management of supraventricular arrhythmia. In overdose cases, flecainide can induce life threatening ventricular arrhythmias and cardiogenic shock. We report the case of a 72-year-old woman admitted to our intensive care unit for a regular monomorphic wide complex tachycardia (QRS duration 240 ms, right bundle branch block and superior axis morphology) without apparent P waves. Clinical examination showed slight left congestive heart failure signs without cardiogenic shock. An intravenous bolus of 10 mg adenosine 5'-triphosphate (ATP) was ineffective to stop the tachycardia. The diagnosis of ventricular tachycardia induced by flecainide overdose was considered. 500 mL of intravenous 84‰ sodium bicarbonate was administrated. The patient's QRS narrowed immediately and 12-lead ECG showed sinus rhythm. Blood samples confirmed the flecainide overdose and the clinical status progressively improved. (Cardiol J 2013; 20, 2: 203–205)

Key words: flecainide, toxicity, overdose, ventricular arrhythmia, ATP

Introduction

Flecainide is a class 1C antiarrhythmic drug used especially for the management of supra-ventricular like atrial fibrillation (AF) [1]. It causes rate-dependent slowing of the rapid sodium channel slowing phase 0 of depolarisation and in high doses inhibits the slow calcium channel [2]. Flecainide also slows conduction in all cardiac fibers, increasing conduction times in the atria, ventricles, atrio-ventricular node and His-Purkinje system. Flecainide can also cause myocardial depression. In overdose cases, flecainide induced life threatening ventricular arrhythmia and cardiogenic shock requiring sometimes extracorporeal membrane oxygenation [3, 4].

Case report

A 72-year-old woman was admitted to our intensive care unit for breathlessness in a context of a regular tachycardia with wide QRS complex. Her medical history included hypertension, paroxysmal AF and a significant psychiatric history. She was treated with flecainide (100 mg twice daily), irbesartan (300 mg daily) and haloperidol (1 mg twice daily). Of note, she had no beta-blocker therapy. Questioning did not find any voluntary drug intoxication. Her general practitioner performed three months ago a 12-lead ECG. It showed sinus rhythm with QTc interval of 400 ms and QRS duration of 100 ms. Before her admission to our intensive care unit, she was given 150 mg of intravenous amio-

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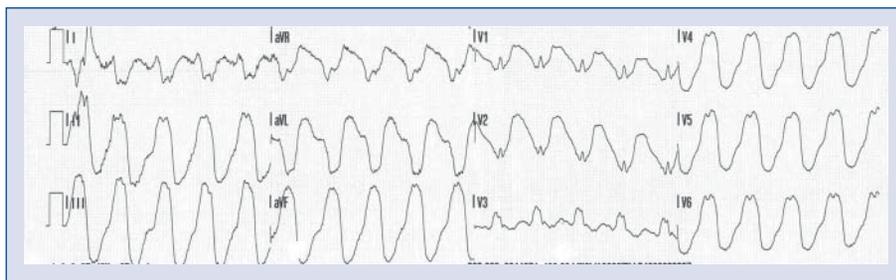


Figure 1. 12-lead ECG displays monomorphic wide complex (QRS duration 240 ms, left bundle branch block inferior axis morphology) tachycardia at 150 bpm without apparent P waves.

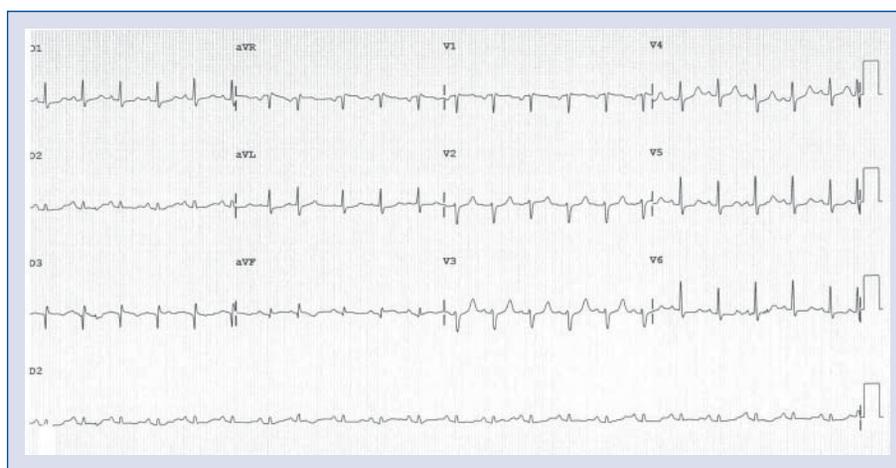


Figure 2. 12-lead ECG demonstrates a sinus rhythm after administration of 500 mL of intravenous 84% sodium bicarbonate.

darone in the emergency room. Clinical examination showed slight left congestive heart failure signs without cardiogenic shock (blood pressure 100/60 mm Hg, oxygen saturation 95%). The 12-lead ECG showed a regular monomorphic wide complex tachycardia at 150 bpm without apparent P wave (Fig. 1). QRS duration was around 240 ms with a left bundle branch block and inferior axis morphology. Transthoracic echocardiography showed a mild left ventricular hypertrophy with a moderate systolic dysfunction (left ventricular ejection fraction 35%), a lack of atrial systole on trans-mitral flow and no valvular disease. An intravenous bolus of 10 mg adenosine 5'-triphosphate (ATP) was used as a diagnostic tool to identify the mechanism of the tachycardia. This administration was ineffective to slow or stop the tachycardia. The diagnosis of ventricular tachycardia induced by flecainide overdose was considered and 500 mL of intravenous 84% sodium bicarbonate was administered. The patient's QRS narrowed immediately following sodium bicarbonate infusion and 12-lead ECG showed sinus rhythm without evidence

of accessory pathway (Fig. 2). Blood samples performed before sodium bicarbonate infusion demonstrated mild metabolic acidosis (pH 7.36, normal 7.37–7.45, arterial lactate 1.60 mmol/L, normal < 1.20), mild renal failure (estimated glomerular filtration rate with MDRD at 42 mL/min), BNP rise (1019 ng/L, normal value < 100) and a flecainide level at 2.13 mg/L (normal therapeutic range 0.2–1 mg/L). Otherwise, troponin I level, blood cells count and serum electrolytes, especially kaliemia, were unremarkable. Clinical status progressively improved. On day 7, transthoracic echocardiography showed a left ventricular ejection fraction improvement up to 50% and the patient was discharged from hospital with a treatment associating amiodarone and irbesartan. One month later, the patient was admitted to our hospital for a check-up. The Holter ECG showed a permanent sinus rhythm without paroxysmal arrhythmias. The coronary angiogram ruled out any coronary artery stenosis. An electrophysiological study demonstrated no inducible ventricular or supraventricular arrhythmias.

Discussion

Flecainide, a class 1C anti-arrhythmic agent, depresses the rate of depolarization of cardiac action potentials producing a membrane stabilizing action. It is a very effective anti-arrhythmic agent against supraventricular arrhythmias, nevertheless flecainide is contraindicated in patients with structural heart disease because it increased mortality [1]. The proarrhythmic effect of flecainide may be related to promoting a reentry in ventricular tissue. The phenomenon is due to a rate-dependent blockade of rapid sodium channels slowing phase 0 of depolarization and an inhibition of the slow calcium channel [2]. In cases of overdose, the mortality with class Ic agents has been reported to approach 22%. Conduction disturbances began with widening of QRS complex which can rapidly progress to ventricular tachycardia, electromechanical dissociation and asystole. The markers of poor prognosis for overdose with membrane stabilizing action drugs are: ingested dose, heart rate > 100 bpm, QRS duration > 100 ms and QT elongation [5]. In the present report, predisposing factors of flecainide toxicity were left ventricular hypertrophy, metabolic acidosis, renal failure (flecainide is mainly excreted in urine), mild heart failure and a likely drug interaction with haloperidol. Of note, we did not find predisposing genetic factors in our patient. Although there are only few successfully treated cases reported [6, 7], hypertonic sodium bicarbonate is considered as a specific antidote to treat flecainide overdose. Hypertonic sodium bicarbonate increases extra cellular concentration of sodium displacing flecainide from its receptors sites. Because flecainide is a weak acid, alkalization may also decrease the active-ionized fraction of flecainide necessary for sodium channels blockade [8]. In our case, sodium bicarbonate infusion significantly reduced QRS duration in few minutes and improved hemodynamic status. This case report tends to confirm the therapeutic efficiency of sodium bicarbonate in a case of moderate flecainide overdose.

ATP can be used as an effective diagnosis tool in identifying the mechanism of wide QRS tachycardia. ATP frequently terminated supraventricular tachycardia, but it had no effect on preexcited

AF or atrial flutter. ATP can also terminated ventricular tachycardia due to triggered-activity or automacity, while ventricular tachycardia related to reentry are insensitive to this drug [9]. Our report supports this data. During flecainide overdose, the mechanism of ventricular arrhythmias is also a ventricular reentry and thus ATP cannot terminate the tachycardia. Hence, ATP is normally considered an antiarrhythmic agent.

Conclusions

We illustrated with our report that ATP is not an effective antiarrhythmic agent to terminate a ventricular arrhythmias due to flecainide toxicity. In this clinical setting, sodium bicarbonate should be preferred.

Conflict of interest: none declared

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