Mediterranean BioMedical Journals
International Journal of Medicine and Surgery
Volume 1, Issue 2, 2014
DOI: 10.15342/ijms.v1i2.18

CLINICAL CASE

NON-ACCIDENTAL FLECAINIDE OVERDOSE A CASE REPORT

Dr Ghannam Abdelilah, MD, Dr Tazi Abdellah, MD, Pr Kettani Ali, MD, Pr Faroudy Mamoun, MD.
Intensive Care Unit of Emergency Trauma Department Ibn Sina Hospital, Rabat, Morocco.

Received 12 July 2014; Revised 11 August 2014; Accepted 06 September 2014.

ABSTRACT
Flecainide acetate is an antiarrhythmic drug used in the treatment of supraventricular arrhythmias. Flecainide causes very rare but often serious intoxications. These intoxications happen either due to a non-accidental overdose or because of a narrow therapeutic index in a patient who suffers from cardiomyopathy or has electrolyte abnormalities. We report an original case of a patient who had taken a high dose of flecainide with the aim of suicide. The patient suffered a cardiogenic shock with complications of lactic metabolic acidosis. Fast diagnosis is essential to reduce the high morbidity and mortality of this intoxication. The treatment plan is symptomatic. It aims at eliminating the poison and compensating cardiac function by treating the shock and the electrolyte imbalances. This allowed us to swiftly regain normal electrical and mechanical cardiac function in our patient. 3 weeks after the psychiatric consultation no sequelae were found. This case highlights that thorough history is essential in order to determine the diagnosis of a drug intoxication since the range of used products is wide. On the other hand, in case of any intoxication, while we apply a specific treatment, a well-managed, systematic, symptomatic treatment is essential to reduce morbidity and mortality.

KEY WORDS: Drug intoxication, flecainide, cardiogenic shock, symptomatic treatment.

Corresponding author:
Dr Ghannam Abdelilah, MD. Intensive Care Unit of Emergency Trauma Department Ibn Sina Hospital, Rabat, Morocco.
Email: ghannamabdelilah@hotmail.com

INTRODUCTION :
Flecainide acetate is classified by Vaughan Williams as a 1c antiarrhythmic drug. It can cause rare but generally serious intoxications with 20 to 40 % mortality rate (1).
This dark prognosis reflects both attempts of suicide committed by taking a high dose, and intoxications caused by the drug's narrow therapeutic index in a patient with fragile health. The severity of this prognosis is accentuated by practitioners' lack of knowledge regarding therapeutic methods, especially as they face this situation rarely.
This study presents a case of massive and isolated absorption of flecainide at a suicidal rate. The patient is a young woman without significant past medical history whose condition has improved under symptomatic treatment.

CASE REPORT:
The patient was a 28-year-old Moroccan woman weighing 60 kg, who had no history of cardiac disease and was not taking any medication regularly. She was admitted to the Emergency Department with drug intoxication 6 hours after having attempted suicide by taking 2 grams of flecainide pills found in the family medicine cabinet. During the examination, she was somnolent with no focal neurological deficits and with normal respiration. She presented with a blood pressure of 110/60 mmHg and a normal pulse of 95 bpm. We

immediately performed gastric lavage, took samples for toxicological screening, and measured the level of flecainide in the plasma. 5 hours after her admission she was in a state of shock presenting with a blood pressure of 80/30 mmHg, bradyarrhythmia of 40 beats per minute, cyanosis in the extremities, a central venous pressure of 22 cmH2O and decreased urine output. Blood work showed lactic metabolic acidosis (pH = 7.24, bicarbonates = 16 mmol/l, pCO2 = 38 mmHg, lactates = 4.7 mmol/l) associated with hypokalemia of 2.6 mEq/l. Qualitative measurement of flecainide in the blood gave a positive result, but the blood level was not determined due to the lack of reagent during the night shift. Treatment was purely symptomatic using nasal oxygen therapy, potassium administered intravenously at a dose of 1 g/h, and atropine at the dose of 1 mg every 5 minutes. Bradycardia reversed after the second dose of atropine, with a HR of 75 beats per minute. Nevertheless, as the state of shock maintained, we had to use dopamine at an increasing dose until 20 mcg/kg/min, as dobutamine was unavailable. The first ECG showed irregular, 280-msec broad ventricular electric complexes without clear atrial activity. Evolution of her state turned quickly favorable as her blood pressure (100/60 mmHg without administering vasopressors) and heart rate (80 beats per minute) became normal. The ECG showed a sinus rhythm with a descreasing width of the ventricular electric complex. The metabolic acidosis and the hypokalemia were resolving. The ultrasound performed 48 hours later was completely normal. Finally, we could not obtain the level of flecainide in the plasma. The patient stayed in the intensive care unit for observation for 48 hours, and then she was treated in the psychiatry department.

DISCUSSION :

Flecainide acetate is classified by Vaughan Williams as a 1C antiarrhythmic drug. It is a membrane stabilizing drug that takes effect by competitive inhibition of the fast sodium channels. It differs from other 1a and 1b class drugs by the fact that it does not change the speed of the repolarization, thus the duration of the action potential. This translates on the electric and hemodynamic level into a decrease of conduction speed in the Purkinje fibres and the myocardial tissue, as well as into a depression of the sinus node function and an increase in the threshold of ventricular pacing. As a final result, it has a negative dromotropic, chronotropic, inotropic and bathmotropic, and also a proarrhythmogenic effect (1).

Flecainide is used in the preventive treatment of documented supraventricular rhythm disorders, notably paroxysmal atrial fibrillations. It is also used in the prevention of recurrence of symptomatic and incapacitating ventricular tachycardias. It is administered by mouth and its bioavailability is approximatively 90%. The peak plasma concentration can be reached in 1 to 3 hours. Even if plasma protein binding is weak (40%), its large volume of distribution (8.3 l/kg) limits the use of the hemodialysis in the elimination of the poision. Metabolism is hepatic, facilitated by cytochrome P450 enzyme, whose activity is subject to genetic variations; in slow metabolizers the drug has a half-life of 12 h, while it is 7 hours in fast metabolizers. There is no first pass hepatic metabolism effect. Elimination is primarily urinary and its 30 to 40% is excreted unchanged (2).

Flecainide intoxications happen most often in patients with cardiomyopathy, electrolyte abnormalities (hypokalemia) or taking a combination of different cardiovascular drugs (digitalis, beta-blocker drugs) (3). This risk is increased by the narrow therapeutic index (rate of therapeutic treatment = 0.2 to 1 ng/ml; toxic > 1 ng/ml; lethal = 2 to 6 ng/ml). Toxic dose is three times higher than the normal drug dose. Moreover, it has to be adjusted downwards in cardiac patients (1, 2). The fact that the patient didn't have any cardiac condition probably helped the fast and complete cardiac recovery.

Flecainide toxicity can present with gastrointestinal and neurological signs related to decreased cerebral blood flow, but most importantly with signs of cardiogenic shock caused by disorders of the cardiac autonomic regulation (bradycardia) and conduction disorders (intraventricular with wide QRS, atrial fibrillation, ventricular premature beats and even ventricular tachycardia, ventricular fibrillation or torsade de pointes by excessive prolongation of the QT) (3-6). One case of flecainide intoxication was reported to result in the appearance of Brugada syndrome by blocking sodium channels (7). Cardiac manifestations appear after 30 to 120 minutes. The higher is the dose, the shorter is the delay (8). In our case, symptoms started 4 hours after ingestion. This delay could not be explained by the available information, therefore the drug level in the plasma would have been necessary to confirm the diagnosis and give a possible prognosis. In our case, diagnosis was determined with the help of the information given by the patient, which were in line with the clinical and paraclinical manifestations (electrocardiogram) at the time of the admission.

Treatment was primarily symptomatic after having removed the toxic agent mostly by gastric lavage. Effectiveness of intestinal dialysis with activated charcoal is controversial (9), while contribution of dialysis is limited by the drug's high volume of distribution. Electrolyte disturbances must be looked for and corrected. Heart failure often demands the use of atropine, catecholamines and even an intra-aortic balloon pump (8). Hypertonic solution of sodium salts is efficient against conduction disorders. As for the electrosystolic stimulation, the membranes' stabilization effect is misleading since it increases the stimulation thresholds.

As for the electrosystolic stimulation, the membrane stabilization effect can be misleading, since it also increases the stimulation threshold.

Prognosis can be favorable after a possible relapse in the following 12 to 36 hours (3). Mortality is approximately 20% (8). There are no established prognostic factors but bradycardia and high flecainide level in the plasma are associated with increased mortality, independent from systolic blood pressure, QRS duration, lactacidemia and perfusion of adrenaline. Our patient had a previously healthy heart and a relatively long delay before the manifestation. All this together with a fast diagnosis based on the history allowed us to start an adequate treatment.

CONCLUSION:

Flecainide intoxication is rare but serious due to the cardiogenic shock that it provokes. Its diagnosis can be difficult in the lack of contributing anamnestic elements. Clinical and paraclinical signs are not specific. Treatment is primarily symptomatic, which gives good results

thanks to the hypertonic solution of sodium salts. Special attention should be paid to prevention, in particular by eliminating contraindications, adapting the dose in patients with multiple comorbidities and we should not forget about psychological support in cases of suicide attempt. Organ donation is possible in the case of brain-dead patients who suffered a flecainide intoxication (10).

PATIENT CONSENT

Written informed consent was obtained from the patient for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

COMPETING INTERESTS

The authors declare no competing interests.

AUTHORS' CONTRIBUTIONS

The participation of each author corresponds to the criteria of authorship and contributorship emphasized in the Recommendations for the Conduct, Reporting, Editing, and Publication of Scholarly work in Medical Journals of the International Committee of Medical Journal Editors. Indeed, all the authors have actively participated in the redaction, the revision of the manuscript and provided approval for this final revised version.

ACKNOWLEDGEMENT

Declared none.

REFERENCES :

[1] Roden DM, Woosley RL. Drug therapy. Flecainide. The New England journal of medicine. 1986;315(1):36.

[2] 2. Jaeger A, Sauder P. Les intoxications par les antiarythmiques de la classe I. Les Intoxications aiguës, Arnette, Paris. 1993:359-73.

[3] 3. Hazouard E, Legras A, Dequin P, Perrotin D. Intoxications graves après ingestion modérée de flécaïnide deux observations. Reanimation Urgences. 1998;7(5):599-602.

[4] 4. André P, Berginiat N, Triaureau G, Lalande G. À propos d'un cas d'intoxication par la Flécaïne< sup>®</sup>. Urgences Medicales. 1997;16(5):205-7.

[5] 5. Son C-W, Lee S-H, Shin D-G, Hong G-R, Park J-S. Acquired long QT syndrome and ventricular tachycardia in a patient on flecainide therapy. Journal of Cardiology Cases.3(3):e137-e42.

[6] 6. CA G. Flecainide. xPharm: The Comprehensive Pharmacology Reference2007. p. 1-7.

[7] 7. Soni S, Gandhi S. Flecainide overdose causing a Brugada-type pattern on electrocardiogram in a previously well patient. The American journal of emergency medicine. 2009;27(3):375. e1-. e3.

[8] 8. Timperley J, Mitchell AR, Brown PD, West NE. Flecainide overdose–support using an intra-aortic balloon pump. BMC emergency Medicine. 2005;5(1):10.

[9] 9. Cabrera Ortega M, Gell Aboy J, Díaz Berto E, Monagas Docasal V, editors. Intoxicación aguda por flecainida. Anales de Pediatría; 2011: Elsevier Doyma.

[10] 10. Vivien B, Deye N, Mégarbane B, Marx J-S, Leprince P, Bonnet N, et al. Extracorporeal life support in a case of fatal flecainide and betaxolol poisoning allowing successful cardiac allograft. Annals of emergency medicine. 2010;56(4):409-12.