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Clinical and Electrocardiographic Particularities of Nebivolol Poisoning

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Abstract

Unlike the third world countries, cardiotropic poisoning is a frequent reason for admission to intensive care in industrialized countries. Those with Nebivolol are poorly described in the literature. The authors report a case of Nebivolol poisoning following a therapeutic error. The clinical examination revealed arterial hypotension, a disorder of consciousness and seizures. The electrocardiogram showed QT prolongation. Treatment consisted of the administration of vasopressive amines, anticonvulsants and correction of fluid and electrolyte disorders. The evolution has been favorable.

Keywords: *Poisoning; Nebivolol; Seizures; Long QT.*

Introduction

Acute intoxication is a common reason for admission to intensive care [1,2]. Those with cardiotropes are not common in third world countries. Beta blockers (propranolol, acebutolol and bisoprolol) are the molecules involved in cardiotropic intoxications [3]. The 3rd generation betabloquant intoxication, nebivolol, is rare because it is a relatively new molecule and little prescribed in our country. The literature describes some cases, all of which occurred for the purpose of autolysis [3,4]. These intoxications are mostly associated with other hypnotic substances or amphetamines). We report a case of Nebivolol intoxication, particularly by its mode of occurrence (therapeutic error) and its monocausal nature.

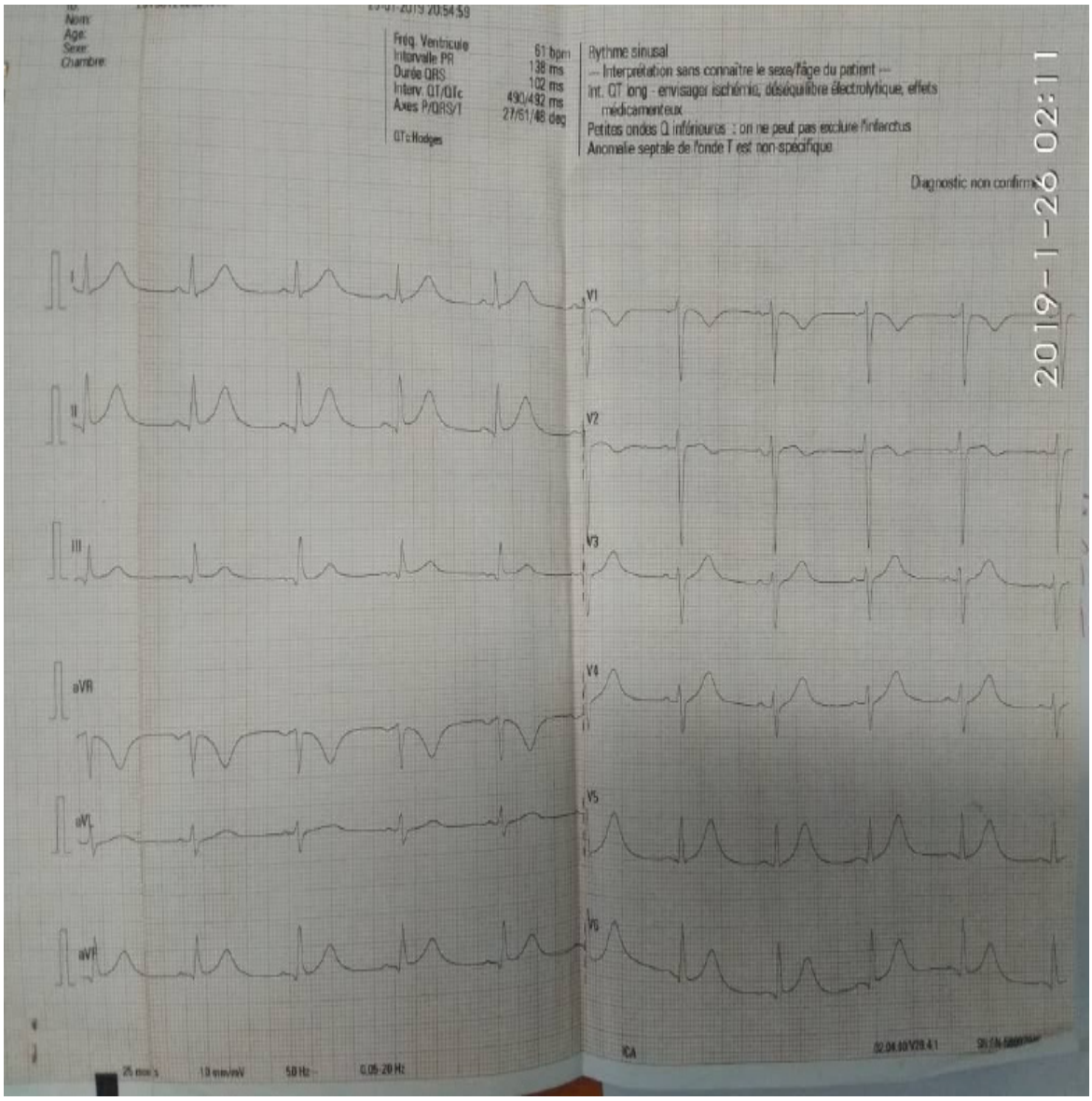
Observation

A 59-year old Caucasian male from Pakistan has been admitted to the Intensive Care Unit for seizures that have been going on for about 6 hours. The interrogation found a notion of hypertension (HT) evolving for about 13 months and treated with Nebivolol 0 5 milligrams (mg) per day and per os from his country of origin. The day before his admission, during a hypertensive crisis (repeated self-measures at home), he ingested 06 tablets Nebivolol 10 mg (6 0mg) in the space of 5 hours. A few hours later, a confusional syndrome, an adynamia and tonic- clonic seizures from the outset became widespread.

The clinical assessment at admission noted a disturbance of alertness (Glasgow score of 12),

isocorous pupils, and brief episodes of psychomotor agitation. There were no signs of intracranial hypertension, no sensorimotor deficit or signs of meningeal irritation. Blood pressure (BP) was 110/60 millimeters of mercury (mmHg) with a pulse at 61 pulses. At cardiac auscultation, the rhythm was steady and there was no breath. Pulmonary and abdominal examination was normal. The hemogram, renal status and ionogram were normal. There was hypophosphoremia, hypocalcemia and hypomagnesemia. The electrocardiogram (ECG) of surface performed indicated an elongation of the QT space (figure 1) and on ultrasound (Figure 2) the cardiac cavities were normal in size with a 51 % ejection fraction (FE).

Treatment consisted of seizure management with Clonazepam combined with Phenobarbital and correction of electrolyte disorders. The evolution was characterizedby the occurrence ofarterial hypotension (PA = 80/40 mmHg) without bradycardia. Dobutamine (7.5 mcg / kg / min IVSE) and Noradrenaline (1mg /h) were rapidly instituted. A few hours after the start of this treatment, the consciousness normalized as well as the hemodynamic state. Vasopressive amines were progressively reduced and stopped after 24 hours. An electrocardiographic control performed after 48h, objectified a normalization of the plot (Figure3). The return home was cleared after 72 hours of hospitalization.



Discussion

This observation reports a Nebivolol intoxication in a 59-year-old hypertensive patient following a therapeutic error. Vasopressive amines, anticonvulsants and the correction of hydro-electrolytic disorders made it possible to treat this patient.

In 86.4% of cases, acute adult intoxications occur in the context of autolysis [1]. Drugs are the main toxic substances (81%) in industrialized countries, as opposed to third world countries where organophosphates are in the first place [1]. The cardiotropic poisonings are therefore not common in black Africa and their frequency is therefore poorly known. In France, cardiotropes the occupy second place of drug poisoning after psychotropic drugs. In 2011, 3 cases of intoxication including Nebivolol (3/911) were recorded [5]. These poisoning with Nebivolol are poorly described because it is a relatively recent molecule. The cases found in the literature, all occurred in a context of autolysis [3, 4], and are associated with other substances (hypnotics or amphetamines) in the majority of cases. Therefore, our observation finds all its originality by the mode of occurrence and the absence of co-ingestion. Indeed, it is not a suicide attempt but rather a therapeutic error. Our patient has successively ingested his tablets in order to obtain normalization of his blood pressure figures. Moreover, the monocausal nature of this intoxication makes it possible to establish a certain causal link between the signs observed and Nebivolol.

cardiovascular signs are at the forefront of cardiotropic intoxication [6]. The drop in blood pressure observed in our patient, is the vasodilator activity of nitric oxide (NO) dependent on the molecule. This vasodilating action is the common property of beta blockers 3rd generation, through α1 receptors. But unlike the others, Nebivolol is devoid of intrinsic sympathomimetic activity. It owes its powerful action to vasodilating β 3 receptors that are the causes of the release of NO [6,7]. Despite their negative chronotropic effect, bradycardia is not always observed in beta-blocking intoxication [8] and is therefore not a pathognomonic sign. This suggests that it is mainly the negative inotropic effect that is mainly responsible for hypotension. As for neurological manifestations, they are related to the lipophilic nature of Nebivolol which allows its passage from the blood-brain barrier. Literature is a case of frequent encephalic signs [7] (severe asthenia, somnolence, coma, convulsions) in beta blocking intoxications. The convulsions commonly observed during propanolol intoxications, have been correlated with the action on the central beta adrenergic receptors. We also hypothesize that the convulsive seizures observed with nebivolol would follow a noradrenergic mechanism mediated by central beta receptors [9] .

Electrocardiographically, Sotalol, Acebutolol and Propanolol are the three beta blockers known to cause QT prolongation [10]. To these could be added Nebivolol as described by our observation. This anomaly would be linked, in our case, to the blockage of the potassium channels resulting in a decrease of the outgoing potassium flow with as a corollary a slowing down of ventricular repolarization. This effect is mostly described with Sotalol. This long QT syndrome is correlated with ionic disorders (hypomagnesemia, hypophosphoremia, hypocalcemia).

Management of beta blocker poisoning includes airway management and the maintenance of satisfactory circulatory cardio function [6]. Arterial gas, as well as invasive blood pressure monitoring could not be available. On the other hand , continuous electrocardiographic monitoring, regular glycemic monitoring and electrolyte dosing were performed. Intubation was not indicated in our patient given the absence of respiratory distress. The ingestion time being greater than 1 hour, the gastric lavage and charcoal were also no longer indicated [6]. We also refrained from administering glucagon (an antagonist of and / or insulin, given the glycemic profile.) In the bradycardias due to beta blockers, the insignificant effect of atropine is justified by the fact that muscarinic receptors do not occur in this context. [6] (hence the use of glucagon). Noradrenaline was used to counterbalance the vasodilator effect of Nebivolol, while Dobutamine was intended to improve the patient's previously unrecognized cardiac performance.

Conclusion

Nebivolol poisoning is not common in the literature. They include both cardiovascular and neurological signs. A long QT syndrome can be observed and requires, in addition to correction of electrolyte disorders, permanent electrocardiographic monitoring. Vasopressive amines have an indisputable place in the management. This intoxication can occur due to a therapeutic error, hence the interest of therapeutic education of patients.

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