Transient sinus dysfunction secondary to lacosamide treatment

Daniel Grados Saso¹, MD; Anyuli Gracia Gutiérrez², MD; Carolina García Arguedas³, MD; Beatriz Toribio Velamazán⁴, MD; Erica León Subías⁵, MD; Claudia Martínez Huguet¹, MD; Rodolfo Reinoso¹, MD; and Francisco Ruiz Montes², MD

¹Cardiology Department; ²Internal Medicine Department; ³Neurology Department; ⁴Emergency Department and ⁵Pneumology Department, from Hospital de Barbastro. Huesca, Spain.

ABSTRACT

The case of an 84-year-old female patient is presented, with a history of high blood pressure, dyslipidemia, chronic venous failure and osteoarthritis, which –due to trigeminal neuralgia– had received treatment with several drugs, without achieving neuropathic pain control; that was why the treatment with lacosamide was started in monotherapy, with an increase in dose until the therapeutic objective was achieved; but the patient presented clinical manifestations and electrocardiographic alterations compatible with sinus dysfunction, which were solved after reducing the dose of the drug.

Keywords: Heart rhythm, Sinus dysfunction, Anticonvulsants, Lacosamide, Adverse effects
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Our report highlights the importance of adequate pharmacological history in all cases of sinus dysfunction and the need for close monitoring in patients taking lacosamide, due to its potential adverse cardiovascular effects.

CASE REPORT

We present the case of an 84-year-old woman with unknown drug allergies or toxic habits; with a history of high blood pressure, dyslipidemia, chronic venous insufficiency, trigeminal neuralgia and osteoarthritis. She was being followed-up by the Cardiology Department for hypertensive heart disease (mild ventricular hypertrophy with preserved ejection fraction). Her last echocardiogram revealed aortic sclerosis with mild regurgitation. Due to her trigeminal neuralgia, she had been previously taking several drugs (gabapentin and amitriptyline) without reaching neuropathic pain control. Hence, she was started on lacosamide monotherapy treatment; the dosing was increased until the patient was completely asymptomatic.

Her regular medication included: olmesartan 40 mg/24h, atorvastatin 10 mg/24h, aspirin 100 mg/24h, omeprazole 20 mg/24h and lacosamide 150 mg every 12 hours and 50 mg at midday. No eye drops or heart rate lowering drugs.

She was admitted from the Emergency Department, referred by her primary care physician who found bradycardia on physical examination and an electrocardiogram (ECG) showing heart rate (HR) of 32 beats per minute (bpm). The patient reported clinical asthenia and progressive dyspnea after three weeks from onset, accompanied by bradycardia (HR

Figure 1. Electrocardiogram on admission to the Emergency Department showing isorrhythmic atrioventricular dissociation with a heart rate of 36 beats per minute.
around 35-40 bpm) in home blood pressure measurement. Bloods showed normal kidney function and normal ion levels (potassium 4.1 mEq/L). Rhythm strip on arrival to the Emergency Department showed isorrhythmic atrioventricular dissociation with HR of 32 bpm (Figure 1), contrasting with the sinus rhythm of 70 bpm seen in a previous ECG, performed two months ago in an outpatient consultation.

At first, she was discussed for consideration of permanent pacemaker implantation but as she was oligosymptomatic and hemodynamically stable it was decided to admit her for observation and clinical assessment.

A possible drug-induced sinus node dysfunction secondary to lacosamide treatment was suspected. Consultation was requested from the Neurology Service, which tailored the dose of lacosamide (reduction to 100 mg every 12 hours), to try to keep the patient asymptomatic from the neurological point of view, without pain due to her trigeminal neuralgia. Echocardiogram 24 hours following admission showed sinus rhythm of 68 bpm, normal PR interval and absence of repolarization alterations (Figure 2). The following day a 24-hour Holter was placed showing: stable sinus rhythm with narrow QRS complex, HR of 62 bpm, maximum of 80 bpm, monomorphic premature ventricular contractions (4%), no ventricular tachycardia, and no significant pauses (the longest was 1.8 seconds).

The patient remained on the hospital ward, with progressive alleviation of symptoms. Asthenia and dyspnea gradually resolved and the ECG prior to discharge revealed sinus rhythm with HR of 72 bpm.

**COMMENTS**

Sinus node dysfunction encompasses a set of disorders compromising the electrical sinus impulse and its transmission via perinodal tissue to the atria. Sinus node dysfunction may have several etiologies and early identification of a potentially reversible cause should always be a primary step in the diagnostic-therapeutic approach. Bradycardia secondary to drug treatment represents up to 21% of cases in some series. Drugs such as lithium and antiepileptics (e.g., phenytoin) are specifically known to cause bradycardia and sinus dysfunction.

Lacosamide is an antiepileptic drug approved by the FDA (Food and Drug Administration) in 2008 and EMA (European Medicines Agency) in 2009. Its mechanism of action is via enhancement of the activation of voltage-gated slow sodium channels. Lacosamide has some adverse effects such as cardiac conduction disorders, and cases of atrioventricular block and sinus dysfunction have been reported in patients using it; those with normal potassium levels receiving high doses of lacosamide have shown sinus pauses and nodal rhythm on the ECG.
A predisposition to bradycardia with the use of antiepileptic drugs such as carbamazepine in elderly women has been suggested due to a possible pre-disposing effect of degenerative impairment of the conduction system\(^6\).

In our case, these electrocardiographic abnormalities were reversed after drug dose tailoring (reduction to 100 mg). The patient had no previous records of sinus dysfunction and was not taking other bradycardia-causing drugs. There was a temporary relationship between increased doses of lacosamide and bradycardia. The patient reported low pain threshold, thus requiring an increase in drug dosage. Ambulatory blood pressure monitoring detected low HF over the preceding days, but she did not seek medical attention. She finally presented to her general practitioner with symptoms of asthenia.

Blood tests revealed normal potassium/other electrolytes levels as well as adequate kidney function. Subsequent ECGs and Holter showed stable sinus rhythm with no significant pauses.

This case highlights the importance of adequate pharmacological history in all cases of sinus dysfunction and the need for close monitoring of patients under treatment with lacosamide due to its potential adverse cardiovascular effects.

**REFERENCES**