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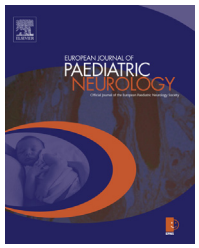

Review article

Late-onset periodic bradycardia during vagus nerve stimulation in a pediatric patient. A new case and review of the literature

Verónica Cantarín-Extremera [a,*], *María-Luz Ruíz-Falcó-Rojas* [a], *Amalia Tamaríz-Martel-Moreno* [b], *Marta García-Fernández* [c], *Anna Duat-Rodriguez* [a], *Belén Rivero-Martín* [d]

[a] *Department of Pediatric Neurology, Hospital Infantil Universitario Niño Jesús, Avd. Menéndez Pelayo 65, 28009 Madrid, Spain*

[b] *Department of Pediatric Cardiology, Hospital Infantil Universitario Niño Jesús, Avd. Menéndez Pelayo 65, 28009 Madrid, Spain*

[c] *Video-EEG Monitoring Unit, Neurophysiology Section, Hospital Infantil Universitario Niño Jesús, Avd. Menéndez Pelayo 65, 28009 Madrid, Spain*

[d] *Department of Pediatric Neurosurgery, Hospital Infantil Universitario Niño Jesús, Avd. Menéndez Pelayo 65, 28009 Madrid, Spain*

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ABSTRACT

Background: Epilepsy is a common disease in the world. Around 10–40% of patients who suffer epilepsy will have intractable seizures. When resective epilepsy surgery is not possible, vagus nerve stimulation (VNS) can be an option. The most common side effects associated with VSN therapy are hoarseness, throat pain and coughing. Cardiac arrhythmia has been reported during lead tests performed during implantation of the device, but few cases during regular treatment. We report a new child where vagally induced bradyarrhythmia, perfectly correlated with the stimulation periods.

Clinical report: 13-year-old girl with refractory myoclonic-astatic epilepsy since the age of two. When she was five years old, a VNS was implanted with complete resolution of her seizures. But when she was 13, she began with sudden falls with loss of consciousness lasting less than 10 s, which were similar to her previous epileptic drop-attacks. Continuous ECG recording was normal but electrocardiography showed a bradycardia of 45 bpm with a syncope-like episode. It was necessary to turn off the VNS.

Conclusions: To our knowledge, there are just three pediatrics and four adults patients described in the literature with this severe and life-threatening side effect. Cardiac complications of VNS therapy are very infrequent but should alert clinicians to its possibility. A

* *Corresponding author*. Tel.: +34 915035900 481.
E-mail addresses: verocantarin@hotmail.com (V. Cantarín-Extremera), mruiz.hnjs@salud.madrid.org (M.-L. Ruíz-Falcó-Rojas), amalia.tamarizmartel@salud.madrid.org (A. Tamaríz-Martel-Moreno), martagf@hotmail.com (M. García-Fernández), annaduatr@gmail.com (A. Duat-Rodriguez).

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cardiac evaluation is mandatory before VNS implantation and periodically thereafter (probably between one or three years).

Contents

1. Introduction

Epilepsy is one of the most common diseases around the world. The prevalence of epilepsy in the pediatric population is 0.5%–1%. Although most patients are successfully treated with one or more antiepileptic drugs (AEDs), treatment-resistant epilepsy occurs in up to one-third of children and can be devastating to children and their families. Severe epilepsy is associated with cognitive decline and can be profound in children, disrupting developmental epochs essential to intellectual and social maturation. If the patient is not a candidate for surgical resection, vagus nerve stimulation (VNS) can be an option.[1]

Dysphonia, throat pain, neck pain or coughing during stimulation are the most commonly reported side effects of VNS. These symptoms typically abate with time or alteration of stimulation parameters.[2,3] Significant or permanent injuries to the vagus nerve or development of dysphagia following implantation are rare (≤4%), infection is in the range of 0%–8% and ipsilateral vocal cord paralysis is another rare side effect.[4] Cardiac complications of VNS are extremely infrequent[5,6] and usually detected in the test performed during the implantation procedure.[7,8] Even so there are seven papers reporting late-onset bradycardia during VNS therapy,[9–15] three of them in pediatric patients.[9,10,12]

2. Clinical report

We report on a 13-year-old girl who begun at the age of 2 (year 2002) with myoclonic seizures and drop-attacks. Despite a thorough workup, no cause was identified. After unsuccessful medical treatment attempts with different AEDs -valproic acid (VPA), clobazam, topiramate, ethosuximide, corticoids … – a VNS was implanted in 2005 without any complication. Her seizures stopped with VNS therapy and VPA, and VNS functioning during the following seven years was uneventful. She had a normal cognition.

When she was 6 years old (in 2008) her father needed cardiac surgery for bicuspid aortic valve and ascending aortic aneurism, and she had a cardiac examination. Her electrocardiogram (ECG) and echocardiography were both normal, with a heart rate of 87 beats per minute (bpm).

Seven years after VNS implantation (January, 2012), she suddenly began to have new attacks with sudden falls and loss of consciousness lasting less than 10 s, which were similar to her previous drop-attacks but preceded by dizziness. Brain magnetic resonance imaging (MRI) was normal. A video-electroencephalography (Video-EEG) showed a normal background activity with some interictal epileptiform abnormalities over right temporal region only during sleep (similar to her previous EEG studies), and some episodes of cardiac arrhythmia were documented on the ECG lead, without any EEG changes. Cardiac examination was normal. The ECG showed a normal sinus rhythm with a heart rate of 90 bpm (beats per minute). But during VNS magnet activation (output current of 1.25 mA) the heart rate slowed down to 45 bpm. The bradycardia duration was a few seconds longer than the stimulation period (30 s). The same response was elicited with magnet VNS activation with an output current of 0.50 mA. The heart rate was not significantly altered when the output current was 0.25 mA (Figs. 1–4). No abnormality was detected in the ECG during the next 24 h, nevertheless we turned the system off on June, 2013.

VNS stimulation parameters had not been changed for the latest years prior to the reported adverse effect (30 s on, 5 min off, 1.25 mA, frequency 20 Hz, pulse width 250 ms).

During the following week the patient did not reveal any presyncopal spells, and she was sent home.

Abnormal placement of electrodes was ruled out by radiography (Fig. 5). We reviewed the routine EEG studies performed in the latest years which confirmed that the ECG had been regular previously.

3. Discussion

Vagus nerve stimulation remains as a viable option for improving seizure control in pediatric patients with epilepsy, but it has some adverse events that we need to know.[1–3]

First of all it is necessary to consider surgical complications, either caused by an infection or by hardware failure, which may imply the need to revise the device or even to

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