

CASE REPORT

Vagus Nerve Stimulation, Sleep Apnea, and CPAP Titration

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Epilepsy and obstructive sleep apnea (OSA) are two relatively common disorders known to coexist and potentially exacerbate each other.¹ Vagus nerve stimulation (VNS) is a currently used, adjunctive treatment for partial epilepsy and is generally well tolerated with few associated side effects. Some of the more common side effects include hoarseness of voice, laryngeal irritation and cough, especially after VNS current increases and the first few weeks of treatment. VNS therapy also affects respiration during sleep and has been shown to worsen preexisting obstructive sleep apnea/hypopnea syndrome (OSAHS) by increasing the number of apneas and hypopneas.² Consistent sleep related decreases in airflow and effort coinciding with VNS activation have been documented, with apneas and hypopneas found to be more frequent during VNS activation than during nonactivation.² VNS may also interfere with effective CPAP titration.

The purpose of this case study was to examine the effects of VNS cycling on CPAP titration for OSA in a patient with medically intractable epilepsy. We found that adequate CPAP titration could not be achieved in the presence of the patient's standard VNS on/off cycling mode. However, when the patient was restudied with his VNS device turned off, a nasal CPAP pressure of 13 cm H₂O resulted in effective treatment of his severe OSAHS. We suggest that polysomnography before VNS implantation should be considered in order to identify patients with OSA.

Keywords: Apnea, epilepsy, CPAP, VNS

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Vagus nerve stimulation (VNS) is an effective nonpharmacological treatment for patients with medically refractory partial onset seizure disorder. More than 50% reduction in seizure frequency rate is achieved in most patients.³ The effects of VNS on sleep were noted when patients with implanted VNS devices and obstructive sleep apnea/hypopnea syndrome (OSAHS) underwent polysomnographic studies. Malow and colleagues were among the first to highlight the frequent coexistence of sleep disordered breathing in patients treated with VNS for epilepsy. In their initial study, they found that patients with VNS had lower airflow and breathing effort after VNS devices were implanted. This was seen during almost every "on" cycle of the devices. Most of the breathing events, were not long lasting or severe enough to be classified as apneas or hypopneas. In follow-up of 2 patients, they found a decrease in apneas and hypopneas when the stimulus frequency was decreased, but not when the intensity, pulse width, or on-time was decreased. They commented that decreasing the stimulus frequency or lengthening the time between stimulations (off period) may reduce the number of these breathing events.⁴ Papacostas et al.⁵ recently presented evidence of VNS induction of central-type sleep apneas. They reported the case of a female patient with medically intractable epilepsy and an implanted VNS device who devel-

oped central-type apneas. Changing the VNS parameters resulted in resolution of these central breathing events and return of the sleep study back to normal.⁵

We describe a patient who presented with sleep disordered breathing, but whose highly medication-resistant epilepsy had improved so dramatically on VNS that we were reluctant to change the chronic stimulation settings. Instead, we modified our CPAP titration for this case, and report the results of that approach.

CASE REPORT

A 54-year-old male, BMI = 39 kg/m² was referred by his epileptologist for a neurological sleep consultation. The patient had a history of medically refractory partial epilepsy for which he had a VNS device implanted in 1998. The device (Cyberonics, Inc. Model # 102) was set to a rapid-cycling mode (current: 1.75 mA, frequency: 30 Hz, pulse width: 500 μ s, cycle: 7 sec on/12 sec off). Compared to pre-implantation seizure frequency (approximately 4 complex partial seizures/month, often with serious injuries), the patient was seizure-free at 6 months with the addition of VNS. Although we are aware that changing VNS parameters may improve sleep disordered breathing,⁴ we were reluctant to change the VNS because of the dramatic improvement of the patient's epilepsy. For patient safety reasons, instead we elected to evaluate and treat for sleep apnea. Sleep history was significant for loud snoring; he denied waking up with a choking or gasping sensation. His wife had never noticed him stop breathing during sleep. The patient typically woke up

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ly 2 months of nightly CPAP use, he returned for a follow-up consultation. He reported feeling much more alert during the day, and he also reported losing 20 pounds. At that time he was scheduled for another CPAP titration with the VNS device on.

Retitration of CPAP with the VNS Cycle On

The results of the follow-up polysomnography with the VNS cycle on showed that at a CPAP pressure of 13 cm H₂O. His AHI was reduced to 13/h, with a lowest SpaO₂ of 94%. The patient was able to sleep for 91 min at this pressure including 16 min of REM sleep. His sleep efficiency, pooling all CPAP pressures tested on this study, was 80%. Total amount of REM sleep was 36 min.

DISCUSSION

Sleep apnea is a common condition, with an estimated prevalence of 4% in men and 2% in women.⁶ Sleep apnea and epilepsy are known to frequently coexist. VNS has been used as an adjunctive treatment in patients with epilepsy since 1997. Recently, it has also received FDA approval as treatment for medically resistant chronic depression. VNS therapy has been shown to worsen preexisting OSAHS by increasing the number of apneas and hypopneas.^{4,5,7-9} Apneas and hypopneas recorded during VNS activation are predominantly obstructive—effort is relatively preserved while airflow is diminished. Apneas and hypopneas occur more frequently during VNS activation than during nonactivation. Both central and peripheral mechanisms have been postulated. Stimulation of peripheral vagal afferents activates motor efferents with cell bodies in the dorsal motor nucleus of the vagus nerve and in the nucleus ambiguus. These efferents may alter neuromuscular transmission to the upper airway muscles of the pharynx and larynx producing upper airway narrowing and obstruction. VNS may also modulate central projections to the brainstem reticular formation altering the rate and depth of respiration. At relatively low current and frequency settings, VNS increases REM sleep, thereby predisposing the patient to apneas and hypopneas.^{7,8} However, a significant difference in REM sleep was not seen between the successful CPAP titrations with or without VNS (36 vs. 35.5 min) in our case.

With the increasing use of VNS as a treatment option, and the known association between VNS and sleep apnea, increased attention needs to be paid to effective ways of treating apnea in patients with comorbid epilepsy and OSAHS. Nasal CPAP remains the most effective treatment for OSAHS. It appears that for some patients at least, attempting nasal CPAP titration with the VNS turned on may prove to be a difficult task. This may be caused by a combination of sleep fragmentation from VNS stimulation and from the anxiety of using CPAP for the first time. Titration of effective CPAP level is classically performed during a full polysomnographic study with the constant attendance of a technician throughout the night. Many patients report poor sleep quality on the night of CPAP titration. Mask related issues, sleeping in unfamiliar surroundings, and frequent adjustments of CPAP pressure may all contribute. Adding to this, sleep fragmentation caused by the VNS stimulation may lead to poorer sleep quality than usual for patients. Therefore, it may be

helpful to initially have the VNS device turned off to help find an effective CPAP pressure. Patients should then be restudied with the VNS device on after they have adapted to the use of CPAP. If increased apneas and hypopneas occur with the VNS turned on, the next step would be to try to abolish them by adjusting VNS stimulation parameters (decreasing the stimulus frequency or by increasing the cycling off-time [e.g., activation every 5 min rather than every 3 min]). Another possibility is to reduce current settings. Our patient was on rapid cycling mode (7 sec on/12 sec off). This frequency is similar to the timing of the apneas and cyclic alternating pattern (CAP). Therefore, it is possible that the VNS stimulation in our patient overlapped the occurrence of sleep apneas, with the rapid cycling mode synchronizing by chance with the CAP rhythm. However, this is very unlikely because the events were time locked throughout the night. If these 2 patterns coincidentally occurred, one would expect that they would desynchronize at some point, and this did not happen. In addition, the patient continued to have severe sleep disordered breathing with the VNS off.

Thus, adjustments to VNS device settings must be undertaken only when one is certain that it indeed is the cause of the sleep related apneic events; otherwise, seizure control may be jeopardized. Achieving the optimal VNS settings to control the patient's seizures and not exacerbate his preexisting OSAHS requires close coordination between the epilepsy specialist and the sleep doctor.

DISCLOSURE STATEMENT

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