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Chronic diarrhea associated with vagal nerve stimulation

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Frequent side effects vagus nerve stimulation (VNS) include hoarseness, cough, and throat pain. Although the vagus nerve physiologically regulates gastrointestinal motility, changes in bowel movement frequency are not included as side effects of VNS. We report a patient who developed chronic diarrhea associated with VNS.

Case report. A 35-year-old man had complex partial seizures since age 14, occurring up to six times per month. Multiple medications including phenytoin, carbamazepine, gabapentin, felbamate, and topiramate did not control the seizures. Intracranial EEG monitoring demonstrated both right and left temporal origin seizures, excluding the patient from consideration for resective surgery and leading to referral for VNS.

After an uncomplicated VNS implantation, the stimulator was set at 0.25 mA/30 Hz/500 ms/30-s on/5-min off/magnet 0.50 mA. The patient was discharged the following day with only a sore throat. One week later, he reported two seizures and an increase in bowel movements. At that time, the stimulator intensity was increased to 0.5 mA and the magnet was increased to 0.75 mA.

Three weeks postimplantation, the patient reported no seizures, but had severe diarrhea consisting of four to five loose bowel movements per day, with exacerbation of preexisting hemorrhoids. Because the patient had no previous history of diarrhea, an association with the VNS was considered, but not found in the literature. Two weeks later, the patient continued to have seizures and frequent watery bowel movements. The stimulator intensity was increased to 0.75 mA, magnet 1.00 mA.

Subsequent anemia led us to perform a full gastrointestinal evaluation, which was significant only for hemorrhoids. A colorectal surgeon was consulted. Because the hemorrhoids were thought to be secondary to the diarrhea, the stimulator was turned off, with the magnet kept on to allow for seizure termination. Three days later, there was a reported reduction in bowel frequency to one to two movements per day.

VNS remained turned off and after 1 month, the diarrhea had completely resolved and the hemorrhoids had improved, postponing planned hemorrhoidectomy. A repeated trial of VNS was initiated, set at an intensity of 0.25 mA. No diarrhea occurred at this setting, but as seizures continued, the stimulus intensity was increased to 0.5 mA. After 1 week, the patient had recurrent diarrhea with loose bowel movements in excess of three per day and excessive bleeding from his hemorrhoids. The VNS was again turned off, with an immediate improvement in his symptoms. He has remained without diarrhea and is awaiting surgical removal of the stimulator.

Discussion. Over 80% of vagal nerve fibers are afferent[1] and it is these fibers that are the presumed target of the VNS. Modulation of gastrointestinal motility occurs through afferent and efferent neurons of the autonomic nervous system. The vagus nerve typically carries afferent signals associated with physiologic regulation of digestion, and efferent signals, which provide the major parasympathetic input to the gastrointestinal system.[2] One function of the efferent fibers is to modulate gastrointestinal motility through enervation of the intestinal musculature. It is known that diarrhea and constipation are associated with conditions of vagal nerve dysfunction, such as diabetic visceral neuropathy or surgical vagotomy.[3] It is therefore conceivable that stimulation of efferent fibers by the VNS may lead to an increase in gut motility and diarrhea.

Experimental stimulation of the vagus nerve at thresholds that excite the population of C-fibers can have the effect of increasing gastric acid secretion and gastric motility.[4] It has been postulated that the lack of parasympathetic visceral side effects during VNS therapy is a result of sparing of C-fibers because of lower threshold stimulation,[5] similar to the lack of respiratory or cardiac side effects seen at this threshold.[4] VNS in humans has not been associated with significant gastrointestinal symptoms, according to currently published data, and analysis of plasma gastrin levels during stimulation showed no significant increase.[6] However, the direct effect of VNS on gastrointestinal motility in humans has never been studied.

We hypothesize that our patient manifested chronic diarrhea as an idiosyncratic response to VNS. It is unclear why this patient responded to the stimulation with diarrhea. It may be that his preexisting hemorrhoids exaggerated a response that has gone undetected in other patients. It is also possible that variability in the number of efferent vagal fibers, or distribution of C-fibers, exists and impacts on the gastrointestinal response to VNS. We believe that clinicians should be aware of diarrhea as a potential side effect of VNS.

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