Vagus nerve stimulation

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Vagus nerve stimulation (VNS) for treatment-resistant depressions: a multicenter study.


Background: Vagus nerve stimulation (VNS) has been used to treat medically refractory seizures in Europe since 1994 and in the US since 1997 (FDA approved for medically refractory partial-onset seizures). A total of 9000 patients have been treated worldwide. VNS may have application for psychiatric disorders, particularly mood disorders. Several observations suggested VNS might alleviate mood disorders: 1) mood improvement in seizure patients with VNS was observed, not accounted for entirely by seizure reduction; 2) PET studies of VNS treated seizure patients show changes in brainstem, limbic and other areas of the CNS that are comparable with antidepressant therapy; 3) most anticonvulsants appear to have some mood stabilizing effects; and 4) in animal models VNS activates neurotransmitters associated with antidepressant activity (i.e. norepinephrine, serotonin, GABA, and glutamate).

AIM: To test the efficacy of VNS for treatment resistant depression.

METHODS: Thirty adult outpatients with non-psychotic treatment resistant depression (n=21), or bipolar I (n=4), or bipolar II (n=5) disorder completed a 12-week, open, unblinded trial of VNS. The first 2-weeks were a recovery period (no stimulation) followed by 10 weeks of VNS (2 weeks VNS adjustment and 8 weeks fixed dose VNS). These patients were on a stable medication regimen, and had failed at least 2 full medication trials or ECT in their current depressive episode.

MAJOR FINDINGS: Response rates were 40% for the HDRS and Clinical Global Impression-Improvement scale and 50% with the MADRS. Of the responders 12 (25%) had MOS SF-36 emotional subscale ratings similar to the general population.

One of the authors (L. B. Marangell) reported at the Pharmacology Update 2000 (a symposium sponsored by Baylor University) that the response rate had risen to 56% and almost all of the original responders had maintained their positive response at 9-month follow-up after the pilot study. Treatment during this follow-up time was not controlled so it is not certain if improvement is related to latent VNS effects or some other variable (i.e. new medication).
Hoarseness was the most common complaint. Throat pain, cough and dyspnea may also occur. These complaints are usually addressed by adjusting VNS early in treatment. Though not reported in this trial or any epilepsy studies, postmarketing surveillance has reported 6 cases of asystole only during the lead test while implanting the VNS device. Most importantly, no cardiac events have occurred outside the implantation procedure.

CONCLUSIONS: Vagal nerve stimulation may be helpful in some patients with severe mood refractory disorders.

LIMITATIONS: This was a small, open, uncontrolled trial, and placebo effects could be powerful.

IMPACT ON INTERNAL MEDICINE: Patients or families may ask about VNS after learning about it through media coverage or the Internet. They can be told it is still an investigational procedure, and only being studied in severe treatment refractory mood disorders. A multisite RCT is currently underway.

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