A case study published in the June Journal of Electroconvulsive Therapy suggests that VNS Therapy may provide cost savings as well as relief from depression in some patients receiving ECT. Ronald L. Warnell, MD, and Nazanin Elahi, MD, of Loma Linda University, California, describe a man in a continuous 6-month episode of severe treatment-resistant depression (TRD) with a history of bipolar I disorder. During initial consultation for ECT while hospitalized for severe suicidal ideation, the 47-year-old was receiving lamotrigine 100 mg/day, venlafaxine extended-release 450 mg/day, ziprasidone 80 mg bid, olanzapine 10 mg hs, lorazepam 1 mg tid prn, lisinopril 20 mg/day, fexofenadine 180 mg/day, atorvastatin 40 mg/day, and levothyroxine 0.125 mg/day. The patient’s initial onset of depression occurred 13 years before this consultation. Since then, he had had at least 2 episodes of manic behavior and repeated episodes of depression, during which he received adequate trials of several selective serotonin reuptake inhibitors; several heterocyclic antidepressants; lithium and other mood stabilizers; antipsychotic agents; and psychotherapy. Over time, medications became less effective, and he was not responding to them at the time of the evaluation.

The patient responded well to the initial series of ECT, as shown by a Montgomery-Åsberg Depression Rating Scale (MADRS) score of 2. The patient then agreed to continuation, and ultimately, maintenance ECT.

Although the patient tolerated ECT, he had short-term memory disturbance. Alterations in electrode placement did not resolve these side effects. The antidepressant effect of ECT was short-lived, with increasing symptoms recurring between 2–3 weeks after treatment.

The patient was very interested in the possibility that VNS Therapy in combination with ECT might permit less frequent ECT, thus reducing memory disturbance and perhaps maintaining a more even mood.

In September 2005, the patient had the VNS Therapy procedure. Maintenance ECT continued, with the VNS Therapy magnet placed over the pulse generator before current was applied. The patient reported improving mood around 2 weeks after activation of the pulse generator. Over the next 3 months, VNS Therapy parameters were adjusted to 30 seconds of stimulation at 30 Hz every 5 minutes, with pulse width at 500 microseconds and output current at 1.50 mA. They have remained at this level. Maintenance ECT sessions were gradually decreased to 1 every 2 months. Within 6 months he showed signs of remission. ECT was then discontinued.

The authors estimated the cost of VNS Therapy at $3,250 over 10 months, prorated from $3,900 annually over the life of the device battery. During the 10 months prior to VNS Therapy, the patient underwent 14 maintenance ECT sessions at a cost of $11,000–$14,000. For 10 months after the initiation of VNS Therapy, the patient had 7 maintenance ECT sessions at a cost of $5,600–$7,000. So the total treatment costs after the addition of VNS Therapy represented a cost savings $2,350–$3,750 during the first 10 months. The authors report that although the benefit in overall functioning was substantial, indirect costs and benefits were not calculated.

Although this study has limited applicability, the authors conclude, “This patient’s marked response and the cost analysis illustrated in this case study present a sensible rationale for clinicians and payers to consider VNS Therapy as a long-term maintenance treatment for patients with TRD.”

The August 2007 online issue of Primary Psychiatry contained a case report of a woman whose response to VNS Therapy has lasted almost 7 years. Thomas L. Schwartz, MD, and Anne Costello, RN, of the State University of New York, Upstate Medical Center and University Hospital in Syracuse, NY, describe Mrs R, a 52-year-old woman whose unipolar major depressive disorder had lasted 11 years without remission.

Upon referral in 2000, Mrs R had many life stressors. Her depression had not remitted despite numerous trials of medications, including fluoxetine, desipramine, and buspirone. Her regimen at referral included sertraline 100 mg/day, buproprion extended-release 300 mg/day, nefazodone 500 mg/day, and mirtazapine 15 mg/day, plus ongoing psychotherapy. She had never attempted suicide or required hospitalization for depression and had refused ECT.

Mrs R had the VNS Therapy procedure in December 2000. Aside from initial voice alteration and cough, which subsided to a manageable level over several months, she experienced no other side effects from the procedure or ongoing treatment with VNS Therapy.

After 16 weeks of VNS Therapy, Mrs R’s score on the 24-item Hamilton Rating Scale for Depression (HAM-D_24) decreased from 33 to 15. She maintained this response for 5 months, had an adjustment disorder lasting 2–3 months, and then returned to a sustained response lasting more than 6 years.

She has continued the medications and psychotherapy. Although she experienced fluctuations in the level of her symptoms, most often related to stressful life events, she had no recurrences of depression. The authors note that this long-term benefit is remarkable for a patient with TRD.

Mrs R and her psychiatrist noted her increased capacity for dealing with stress. She described an “evenness of mood” that she had not felt since before her initial diagnosis. The patient stated that her depressive symptoms, social functioning, and quality of life were “on average 60% to 70% better” with VNS Therapy.

This article is CME-accredited by joint sponsorship of the Mount Sinai School of Medicine and MBL Communications, Inc.

Susan: a VNS Therapy case history

Patient history

• 59-year-old English professor
• Diagnosis: major depressive episode (1983)
• Duration of illness: 24 years
• Family history of depression
• Worsening depression precipitated by deaths of mother and only child in 1990

Medication and treatment history

• Prozac, lithium provided good results, which faded after 4–5 months
• Other medications: bupropion, methylphenidate, atypical antipsychotics, anxiolytics
• Psychotherapy begun in 1983
  – Initially 4 hours/week for 4.5 years
  – Currently every 2 weeks

Implanted with VNS Therapy—May 2001

• Device activated August 2001

Outcomes

• December 2001: notes “gradual uptick” in mood
• Current remission sustained ≥6 years
• Patient returned to work part-time in January 2007
• Current medications: Buproprion sustained-release 200 mg bid, methylphenidate 20 mg tid, aripiprazole 5 mg qd, clonazepam 0.25 mg tid; a considerable reduction from previous regimens

What approaches have you found to be particularly effective in obtaining coverage for your patients?

There is no question that the biggest obstacle we currently face in offering VNS Therapy to our patients is obtaining adequate insurance coverage. This became substantially more difficult with the noncoverage determination issued by Medicare this May. While we are still hopeful that this decision will be reevaluated and VNS Therapy will be available to our Medicare patients in the future, it complicates our ability to provide this treatment today.

My colleagues at the Family Life and Learning Center and I have been fortunate with approvals for our patients. I currently treat over 40 patients with VNS Therapy. Many of these patients have commercial (or private) insurance. We are impressed by their response rates and have seen dramatic improvements. In our area I work very closely with the Regional Access Manager from Cyberonics. We have jointly presented clinical data to medical directors of regional insurance carriers and have succeeded in getting approvals once these medical directors are more aware and educated about TRD and VNS Therapy.

I also document as much as possible of the clinical history of TRD at our initial request for coverage. It helps to include prior hospitalizations, ECT treatments, medication failures, and suicide attempts, and to quantify the cost of unsuccessful treatments. If the initial request is denied, however, the Cyberonics Regional Case Managers offer a helpful service: they assist us in filing the various stages in the appeal process. Persistence can certainly pay off.

VNS Therapy is an invaluable treatment option for the more severe cases of depression that I treat. To offer this to your patients, it may help to partner with your Regional Access Manager and Regional Case Manager to coordinate your efforts to provide coverage. This works effectively for us and allows us to offer this treatment to many more patients.
Bibliography

- A review of the use of VNS Therapy in resistant depressive disorder and discussion of other possible uses

- A systematic review of 47 randomized studies of adults with treatment-resistant or refractory unipolar major depression showed a clear need for a consistent framework of concepts and methods for investigating TRD

- A review of VNS Therapy, transcranial magnetic stimulation, and deep brain stimulation, with an emphasis on TRD

- VNS Therapy is associated with ventro-medial prefrontal cortex deactivation corresponding to the antidepressant response

- A brief review of the definitions, prevalence, and various treatment options for TRD, including switching, augmentation, combination therapies and nonpharmacologic treatments

- In 14 patients receiving VNS Therapy for >2 years, highly significant weight loss was observed proportional to initial BMI, not correlated with mood symptoms, and without reported dieting or exercise

- A review of mechanism of action and current and potential future uses of VNS Therapy

- A review of VNS Therapy for psychiatric nurses

- See page 2

- See page 1

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Prescribing physicians should be experienced in the diagnosis and treatment of depression or epilepsy and be familiar with the programming and use of the VNS Therapy System.

Physicians who implant the VNS Therapy System should be experienced performing surgery in the carotid sheath and should be trained in the surgical technique relating to implantation of the VNS Therapy System.

The safety and effectiveness of the VNS Therapy System have not been established for use during pregnancy, lactation, or in children under the age of 12 years. VNS should be used during pregnancy only if clearly needed.

The VNS Therapy System is indicated for use only in stimulating the left vagus nerve in the neck area inside the carotid sheath. The VNS Therapy System is indicated for use only in stimulating the left vagus nerve below where the superior and inferior cervical branches separate. The VNS Therapy System is for use only in stimulating the left vagus nerve.

It is important to follow infection control procedures. Infections related to any implanted device are a concern and may require that the device be explanted. The patient should be given antibiotics prophylactically. The surgeon should ensure that all instruments are sterile prior to the procedure.

The VNS Therapy System may affect clinician, device, and pacemaker therapies. It can impair or interfere with the programming of other implantable cardiac pacemakers and implanted defibrillators. Possible effects include sensing problems and inappropriate device responses. If the patient requires concurrent implantable pacemaker, defibrillator therapy or other types of stimulators, careful programming of each system may be necessary to optimize the patient's benefit from each device.

Reversal of Lead polarity has been associated with an increased chance of bradycardia in animal studies. It is important that the electrodes are attached to the left vagus nerve in the correct orientation. It is also important to make sure that Leads with dual connector pins are correctly inserted (white marker band to + connection) into the Pulse Generator's Lead receptacles.

The patient can use a neck brace for the first week to help ensure proper Lead stabilization. The patient should not program the VNS Therapy System to an "ON" or periodic stimulation treatment for at least 14 days after the initial or replacement implantation.

Do not use frequencies of 5 Hz or below for long-term stimulation. Resetting the Pulse Generator turns the device OFF (output current = 0.0 mA), and all device history information is lost.

Patients who smoke may have an increased risk of laryngeal irritation. Smoking can cause hypoventilation and atelectasis.

Patients should exercise caution in avoiding devices that generate a strong electric or magnetic field. If a Pulse Generator ceases operation while in the presence of electromagnetic interference (EMI), moving away from the source may allow it to return to its normal operation.

The VNS Therapy System operation should always be checked by performing device diagnostics after any of the procedures mentioned in the physician's manuals.

For clear imaging, patients may need to be specially positioned for mammography procedures, and a different location of the Pulse Generator in the chest may be necessary.

Therapeutic radiation may damage the Pulse Generator's circuitry, although no testing has been done to date and no definitive information on radiation effects is available. Sources of such radiation include diagnostic and therapeutic radiation, cobalt machines, and linear accelerators. The radiation effect is cumulative, with the total dosage determining the extent of damage. The effects of exposure to such radiation can range from a temporary disturbance to permanent damage, and may not be detectable immediately. External defibrillation may damage the Pulse Generator.

Use of electrotherapy [cathode or radio frequency (RF) ablation devices] may damage the Pulse Generator.

Magnetic resonance imaging (MRI) should not be performed with a magnetic resonance body coil in the same transmit mode. The heat induced in the Lead by an MRI body scan can cause injury. If an MRI should be done, use only a transmission-receive type of head coil. MRI compatibility was demonstrated using a 1.5T General Electric Signa Imager with a Model 100 only. Use caution when other MRI systems are used, since adverse device effects may occur because of different magnetic field distributions. Consider other imaging modalities when appropriate.

Procedures in which the radio frequency (RF) is transmitted by the body coil should not be done on a patient who has the VNS Therapy System. If the procedure requires use of leads, protocols must not be used that utilize local coils that are RF receive-only, with RF-transmit performed by the body coil. Note that some RF coils are receive-only, and that most other local coils, such as knee and spinal coils, are also RF-receive only. These coils must not be used in patients with the VNS Therapy System.

Extraocular shockwave lithotripsy may damage the Pulse Generator. If therapeutic ultrasonic therapy is required, avoid positioning the area of the body where the Pulse Generator is implanted in the water bath or in any other position that would expose it to ultrasound therapy. If that positioning cannot be avoided, program the Pulse Generator to "Off" and then, during the therapy, reprogram the Pulse Generator to the original parameters.

Routine therapeutic ultrasonic could damage the Pulse Generator and may be inadvertently concentrated by the device, causing harm to the patient.

For information related to home occupational environments, cellular phones, other environmental hazards, and electronic devices, the Cyberonics engineers, please refer to the physician's manuals for complete information.

1. The information contained in this Brief Summary for Physicians represents partial excerpts of important prescribing information from the physician's manuals. (Copies of VNS Therapy physician and patient's manuals are posted at www.VNSTherapy.com/manuals.) The information is not intended to serve as a substitute for a complete and thorough understanding of the material presented in all of the physician's manuals for the VNS Therapy System and its component parts nor does it give the manufacturer's full disclosure of all patient information concerning the use of this product, potential safety complications, or efficacy outcomes.

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